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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.

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NIKOLAI ALEXANDROVICH MENSHUTKIN

D. N. Monastyrskii

(Fiftieth Anniversary of his death)

1907 is a year to be remembered by chemists, as five outstanding scientists died in the first three months of that year and among them were two Russians: D. I. Mendeleev and N. A. Menshutkin.

Nikolai Alexandrovich Menshutkin devoted a large part of his life (October 24, 1842 – February 5, 1907) to St. Petersburg University, where he finished the course in 1862; it was only in 1902 that he left the University and took over at the reopened St. Petersburg Polytechnic Institute as professor of analytical and organic chemistry.

We will not dwell on all the stages of Menshutkin's life, as they are quite well known from the records of the meetings of the Russian Physical and Chemical Society's Chemistry Section* and especially from the biography written by his son, B. N. Menshutkin.**

Menshutkin was well known as a scientist both in Russia and abroad. He was best known for his work in the fields of organic and physical chemistry. Having started with a study of esterification, he improved upon and further developed the work done before him by M. Berthelot and Pean de St. Giles. The Zurich professor, Karrer, noted in the table "Historical data on important discoveries in the field of organic chemistry" in the appendices of his text book,*** under the year 1877, "Discovery of the laws of esterification (Menshutkin)."

Another series of classical works by Menshutkin is devoted to the effect of so-called inert solvents on the rate of a reaction. The last of this series was carried out in the Polytechnic Institute.

The first congress of Russian naturalists took place in 1867. The chemists attending this conference decided to organize a Russian Chemical Society and its statute was ratified on October 26, 1868. The Society started its activities in 1869 with a body of 35 members in all, among them the famous trio: Mendeleev, Butlerov and Menshutkin. From the very first year, the "Journal of the Russian Chemical Society" was issued under Menshutkin's editorship. Starting with Volume V (1873), this journal began to publish the papers of members of the then recently established Physical Society and the journal was renamed "Journal of the Russian Chemical and Physical Society." Two years later, at the suggestion of D. I. Mendeleev, the two societies combined and the journal was to be known till its termination as the "Journal of the Russian Physical and Chemical Society" with two sections – one chemical and the other physical. The responsible post of editor of this journal, famous in the annals of Russian science, was occupied for 31 years by N. A. Menshutkin. At the meeting of the Chemistry Section on October 5, 1900, he announced that he was no longer able to continue his duties as editor and requested that the question of selecting a successor be raised at the next November meeting. Opening this meeting, the chairman, Academician N. N. Beketov, gave a short speech mentioning the great services N. A. Menshutkin had rendered to the society and ended with the words: "The Society is under the moral obligation to honor these useful services of its respected fellow member."

Responding to this appeal, the Chemistry Section chose a special commission and on its advice, decided to 1) retain the name of N. A. Menshutkin on the title page of the J. Russ. Phys. Chem. Soc., adding a new phrase to the title: "Under the editorship of N. A. Menshutkin from 1869 to 1900"; 2) add the portrait of N. A. Menshutkin to the first issue of the Journal in 1901; and 3) publish in the same issue the speech mentioned above by Acad. N. N. Beketov.

*J. Russ. Chem. Soc., 39, 241-304 (1907).

** Life and Works of Nikolai Alexandrovich Menshutkin. Bull. St. Peters. Polytechnical Inst., 8, No. 2 (1907).

***P. Karrer, A Course in Organic Chemistry, Vol. II, 956, Moscow (1938) (Russian translation).

In the field of teaching, N. A. Menshutkin is known not only as a lecturer of organic chemistry but also as the professor who first organized the really scientific teaching of analytical chemistry. His famous text book, "Analytical Chemistry," was not only a reference book for many generations of Russian chemists, but was also translated into foreign languages: three German editions and one English edition were published.

Toward the end of his life, Menshutkin repeated his university experiment in the Polytechnic Institute: not limiting himself only to lectures, he conducted regular discussions with the students on analytical subjects and their knowledge was judged at the end of the semester by the results of these discussions. Such a personal participation of the professor had a great educational effect both on the students and on the assisting staff.

At a meeting on May 15th-16th, 1957, the Leningrad section of the All-Soviet D. I. Mendeleev Chemical Society recorded the 50th Anniversary of the death of outstanding chemist N. A. Menshutkin, who had been an active member of the society.

DERIVATIVES OF BICYCLO(1,2,2)HEPTANE

III. 2-ACYLBICYCLO(1,2,2)HEPTENES-2 AND SOME OF THEIR REACTIONS

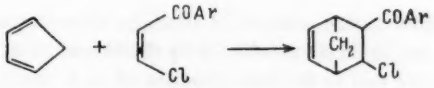
N. K. Kochetkov and A. Ya. Khorlin

As was shown previously in our laboratory [1-3], 2-acyl-3-chlorobicyclo(1,2,2)heptanes have a labile chlorine atom which is readily exchanged for an alkoxy, acetoxy or amino group and reacts with compounds containing an active methylene group. The high lability of the chlorine atom, which is characteristic of all β-halogen-substituted ketones, is also present in 2-acyl-3-chlorobicyclo(1,2,2)heptanes, which have a rigid bicyclic system.

This report is devoted to the study of the dehydrochlorination of these compounds resulting in the formation of previously almost unknown α, β-unsaturated ketones of the bicycloheptane series, 2-acylbicyclo(1,2,2)-heptenes-2, which may be of interest in the further development of syntheses in the bicyclo(1,2,2)heptane series. The only example of this class – 2-acetylbicyclo(1,2,2)heptene-2 was prepared [1] by treating 2-acetyl-3-chlorobicyclo(1,2,2)heptane with dilute aqueous alkali. However, this method has a number of disadvantages and it cannot be recommended as a general method for synthesizing compounds of this type.

We have now developed a new, general and more convenient method for dehydrochlorinating 2-acyl-3-chlorobicyclo(1,2,2)heptanes.

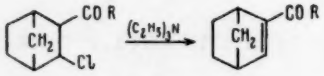
The starting 2-acyl-3-chlorobicyclo(1,2,2)heptanes were prepared by the method we described previously i.e., by condensation of β-chlorovinyl ketones with cyclopentadiene [4] followed by hydrogenation of the double bond in the adducts [1, 2]. We have now also studied the diene synthesis of β-chlorovinyl ketones of the aromatic series, which have also become generally available [5]. As might be expected, aryl β-chlorovinyl ketones containing a substituent (CH_3 group, chlorine atom, nitro group) in the aromatic nucleus, reacted smoothly with cyclopentadiene to give the corresponding 2-aroyl-3-chlorobicyclo(1,2,2)heptenes-5 in high yields:



Ar=p-$CH_3C_6H_4$, p-ClC_6H_4, p-$O_2NC_6H_4$

Hydrogenation of 2-acyl-3-chlorobicyclo(1,2,2)heptenes-5, either with an aromatic or an aliphatic radical, proceeded quite smoothly over palladium on barium sulfate and, in contrast to the procedure described earlier [4], we used dry acetone as solvent. This allowed a more rapid hydrogenation, which thus decreased the inevitable hydrogenolysis of the chlorine atom in the adducts since this reaction became noticeable when hydrogenation was slowed down as occurred in using such solvents as alcohol and ether and with batches of 2-acyl-3-chlorobicyclo heptenes greater than 0.3-0.5 mole. Hydrogenation should be stopped immediately after the absorption of the exact theoretical amount of hydrogen as further hydrogenation results in contamination of the 2-acyl-3-chlorobicyclo(1,2,2)heptane with traces of the difficultly separable 2-acylbicyclo(1,2,2)heptane.

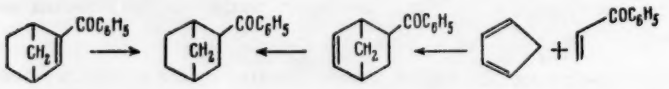
We dehydrochlorinated 2-acyl-3-chlorobicyclo(1,2,2)heptanes by treating them with triethylamine. This reagent is better than dilute alkali [1] as with it the reaction occurs in a homogeneous medium which, in its turn, decreases the resinification of the α,β-unsaturated ketone formed. In order to decrease this process to a minimum, it is most convenient to dehydrochlorinate by heating a mixture of the chloroketone and triethylamine in dry benzene for several hours. This method gave 2-acylbicyclo(1,2,2)heptenes-2 in yields of 50-75%.



R=CH3, C2H5, C3H7, C6H5, p-ClC6H4

The structure of the compounds obtained by this method was proved by their properties. They decolorized a permanganate solution and absorbed about 1 mole of hydrogen when hydrogenated. The conjugated position of the double bond in relation to the carbonyl group was confirmed by the absorption maxima* of their 2,4-dinitrophenylhydrazones (λ_{max} = 369-370 mμ), which are characteristic of α,β-unsaturated ketones [6].

A detailed investigation of the dehydrochlorination of 2-benzoyl-3-chlorobicyclo(1,2,2)heptane showed, however, that in this case the reaction was not well-defined. Two crystalline substances with m. p. 80-81 and 131-132° were isolated from the reaction mixture. The low melting substance was found to be the product of normal dehydrochlorination – 2-benzoylbicyclo(1,2,2)heptene-2. It decolorized permanganate and had an absorption maximum (λ_{max} = 253.8 mμ ; log ε 3.2) characteristic of an α,β-unsaturated ketone. Its structure was proved by hydrogenation to 2-benzoylbicyclo(1,2,2)heptane, which was found to be identical in its 2,4-dinitrophenylhydrazone to the hydrogenation product of 2-benzoylbicyclo(1,2,2)heptene-5 [7]; we simplified and improved the preparation of the latter (see Experimental).

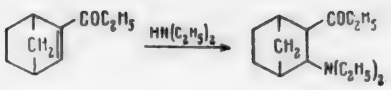


The second substance with m. p. 131-132° did not contain a multiple bond (it was not hydrogenated and did not decolorize permanganate) and its absorption spectrum did not have a maximum characteristic of an α,β-unsaturated ketone. Although it has not been studied more thoroughly it may be considered as the dimer of 2-benzoylbicyclo(1,2,2)heptene-2. It should be noted that in dehydrochlorinating 2-p-chlorophenyl-3-chlorobicyclo(1,2,2)heptane, we also isolated a very small amount of a saturated substance.

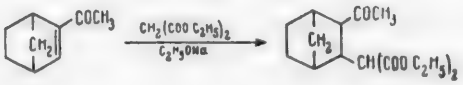
In connection with the dehydrochlorination products of aliphatic chloroketones (2-acetyl-, 2-propionyl-, 2-butyroyl-3-chlorobicycloheptanes), we could not prove clearly the existence of saturated derivatives similiar to those named above. It should be noted that in the hydrogenation of α,β-unsaturated ketones, we invariably observed incomplete hydrogen absorption (by 10-15% less, see also [1]). However, this phenomenon could be due to the spontaneous polymerization of these compounds during hydrogenation, as in preparing the 2,4-dinitrophenylhydrazones of unsaturated ketones, we always isolated only one substance and, in spite of a thorough search, we could not find the isomeric 2,4-dinitrophenylhydrazones. This indicated that the samples of aliphatic 2-acylbicyclo(1,2,2)heptenes-2 prepared by us did not contain much impurity.

It seemed interesting to elucidate the problem of the activity of the multiple bond in the α,β-unsaturated ketones we prepared, which contained a rigid bicyclo system. Investigation showed that the double bond activity of these compounds did not differ from that of the usual α,β-unsaturated ketones. Thus they added amines readily as was shown by the reaction of 2-propionylbicyclo(1,2,2)heptene-2 with diethylamine, which gave 2-propionyl-3-diethylaminobicyclo(1,2,2)heptane which we had prepared previously [3].

* V. G. Vinokurov plotted the absorption spectra in the ultraviolet region on SF-4 and ISP-22 spectrometers and the authors thank him for his work.



2-Acylbicyclo(1,2,2)heptenes-2 underwent a Michael condensation. Thus, 2-acetylbicyclo(1,2,2)heptene-2 condensed with malonic ester to give 2-acetylbicyclo(1,2,2)heptyl-3-malonic ester, which we described previously [2].



In conclusion, we should note that the reaction product yields in the last two cases were higher than in the direct substitution of a chlorine atom in 2-acylbicyclo(1,2,2)heptanes [2, 3], and this method does not have advantages, in spite of the extra stage.

EXPERIMENTAL

Synthesis of 2-Acyl-3-Chlorobicyclo(1,2,2)Heptenes-5

2-Acetyl-, 2-propionyl-, 2-butyroyl- and 2-benzoyl-3-chlorobicyclo(1,2,2)heptenes-5 were prepared as described previously [2, 4].

2-p-Toluyl-3-chlorobicyclo(1,2,2)heptene-5. 5.0 g (0.028 mole) of p-tolyl-β-chlorovinyl ketone, dissolved in 5 ml of petroleum ether, was mixed with 5.3 g (0.08 mole) of cyclopentadiene. Next day the crystals of adduct were filtered off and recrystallized from ethyl acetate. The yield was 5.1 g (75%), m. p. 91.5-92°.

Found %: C 73.04, 73.21; H 6.26, 6.13; Cl 14.68, 14.67. $C_{15}H_{15}OCl$. Calculated %: C 73.02; H 6.13; Cl 14.39.

The colorless crystals were readily soluble in benzene, acetone and hot alcohol and moderately so in ether.

2-p-Chlorobenzoyl-3-chlorobicyclo(1,2,2)heptene-5 was synthesized similarly from 6.5 g (0.033 mole) of p-chlorobenzoyl-β-chlorovinyl ketone and 8.0 g (0.12 mole) of cyclopentadiene in 6 ml of petroleum ether. The yield of pure material was 7.0 g (80%), m. p. 94.5-95° (from ethyl acetate).

Found %: C 63.36, 63.25; H 4.58, 4.47; Cl 26.81, 26.73. $C_{14}H_{12}OCl_2$. Calculated %: C 62.94; H 4.53; Cl 26.54.

The colorless crystals were readily soluble in benzene and acetone and less soluble in alcohol and ether.

2-p-Nitrobenzoyl-3-chlorobicyclo(1,2,2)heptene-5. 4.0 g (0.061 mole) of cyclopentadiene was added to 3.0 g (0.014 mole) of p-nitrophenyl-β-chlorovinyl ketone in 8 ml of ethyl acetate. Next day the crystalline adduct was filtered off and recrystallized from glacial acetic acid. The yield was 3.0 g (76%), m. p. 147-148°.

Found %: C 60.62, 60.57; H 4.36, 4.31; Cl 12.85, 12.66. $C_{14}H_{12}O_3Cl$. Calculated %: C 60.57; H 4.36; Cl 12.77.

The golden yellow crystals were readily soluble in benzene, moderately so in ethyl acetate and difficultly soluble in petroleum ether.

Synthesis of 2-Acyl-3-Chlorobicyclo(1,2,2)Heptanes

The hydrogenation of 2-acetyl-, 2-propionyl-, 2-butyroyl- and 2-benzoyl-3-chlorobicyclo(1,2,2)heptenes-5 was carried out over palladium on barium sulfate (6% palladium) as described previously [4], using

anhydrous acetone as the solvent. Substitution of ether or alcohol [4] for the acetone made faster hydrogenation possible; the yields were 90-95% with charges of 0.3-0.5 mole.

Hydrogenation of 2-p-chlorobenzoyl-3-chlorobicyclo(1,2,2)heptene-5 gave a quantitative yield of 2-p-chlorobenzoylbicyclo(1,2,2)heptane, m. p. 109-109.5° (from alcohol).

Found %: C 62.20, 62.27; H 5.33, 5.34. $C_{14}H_{14}OCl_2$. Calculated %: C 62.47; H 5.24.
The colorless crystals were readily soluble in acetone and benzene and poorly soluble in alcohol and petroleum ether.

Synthesis of 2-Acylbicyclo(1,2,2)Heptenes-2

2-Acetyl-bicyclo(1,2,2)heptene-2. 40.0 g (0.43 mole) of 2-acetyl-3-chlorobicyclo(1,2,2)heptane in 60 ml of dry benzene was mixed with 100 ml of triethylamine, a small amount of hydroquinone added and the mixture boiled gently on a water bath for 20-25 hours. The precipitated crystals of triethylamine hydrochloride were filtered off and washed with ether on the filter. The solvent and triethylamine were distilled off from the mother liquors and the residue distilled in vacuum to give a fraction with b. p. 62-66° (3-4 mm); the yield was 30.8 g (50%), n_D^{20} 1.4979; d_4^{20} 1.0141. After 2 distillations the substance had:

B. p. 76-78° (5 mm), n_D^{20} 1.4992, d_4^{20} 1.0102 RM_D 39.86. $C_9H_{12}O$ F. Calculated: 38.92; EMR_D 0.94.

Literature data [1]: b. p. 54-56° (2 mm), n_D^{20} 1.4972, d_4^{20} 1.0018.

Found %: C 79.40, 79.50; H 8.85, 8.84. $C_9H_{12}O$. Calculated %: C 79.47; H 8.88.
The colorless mobile liquid had a sharp smell and a weak lacrimatory effect and quickly polymerized on storing.

The 2,4-dinitrophenylhydrazone of 2-acetylbicyclo(1,2,2)heptene-2 was prepared in glacial acetic acid; the bright red crystals had m. p. 153° (from glacial acetic acid), λ_{max} 369 mμ (in methanol).

2-Propionylbicyclo(1,2,2)heptene-2 was synthesized similarly from 26.5 g (0.14 mole) of 2-propionyl-3-chlorobicyclo(1,2,2)heptane, which was boiled with a mixture of 90 ml of triethylamine and 50 ml of benzene for 6 hours, The yield was 16.2 g (77.4%).

B. p. 59-60° (2 mm), n_D^{20} 1.4950, d_4^{20} 0.9965, MR_D 43.96. $C_{10}H_{14}O$ F. Calculated: 43.52; EMR_D 0.44.

Found %: C 79.59, 79.45; H 9.19, 9.30. $C_{10}H_{14}O$. Calculated %: C 79.59; H 9.39.
The colorless, mobile liquid had a characteristic sharp smell. It polymerized on storing.

The 2,4-dinitrophenylhydrazone of 2-propionylbicyclo(1,2,2)heptene-2 was prepared in glacial acetic acid and recrystallized from the same solvent; the bright red crystals had m. p. 145.5-146°, λ_{max} 369-370 mμ (in methanol).

Found %: N 16.86, 16.92. $C_{16}H_{18}O_4N_4$. Calculated %: N 16.96.

2-Butyroylbicyclo(1,2,2)heptene-2 was synthesized similarly from 53.0 g (0.265 mole) of 2-butyroyl-3-chlorobicyclo(1,2,2)heptane and 200 ml of triethylamine in 100 ml of benzene; the yield was 32.5 g (74.2%).

B. p. 82-84° (3 mm), n_D^{20} 1.4915, d_4^{20} 0.9861, MR_D 48.25. $C_{11}H_{16}O$ F. Calculated: 48.14; EMR_D 0.11.

Found %: C 80.29, 80.38; H 10.36, 10.54. $C_{11}H_{16}O$. Calculated %: C 80.48; H 9.99.
The colorless liquid with a characteristic sharp smell polymerized on storing.

The 2,4-dinitrophenylhydrazone of 2-butyroylbicyclo(1,2,2)heptene-2 was prepared in glacial acetic acid and recrystallized from the same solvent; the bright red crystals had m. p. 129-130°, λ_{max} 369-370 mμ (in methanol).

Found %: N 16.06, 16.22. $C_{17}H_{20}O_4N_4$. Calculated %: N 16.27.

2-Benzoylbicyclo(1,2,2)heptene-2. A mixture of 20.0 g of 2-benzoyl-3-chlorobicyclo(1,2,2)heptane and 80 ml of triethylamine was boiled for 10 hours, and the precipitated crystals of triethylamine hydrochloride

filtered off and washed with ether; the solvent was distilled off from the mother liquors and the residue poured into 2% sulfuric acid. The oil precipitated crystallized after 1-2 hours. The crystalline substance thus obtained was filtered off, washed on the filter with dilute sodium carbonate solution and water and dried; the weight was 15.0 g and the m. p. 58-61°. The substance was dissolved in ether and the ether solution filtered and cooled to − 70°, when crystals precipitated (8.1 g, 46.5%), which had m. p. 78-79°; a second recrystallization from ether or acetone at − 70° raised the melting point to 80-81°, which remained constant after additional recrystallizations; λ_{max} 253.8 mμ; log ε 3.2 (in methanol).

Found %: C 84.48, 84.56; H 7.29, 7.30. $C_{14}H_{14}O$. Calculated %: C 84.82; H 7.17.
The colorless crystals were readily soluble in alcohol, ether, acetone, benzene and petroleum ether. They decolorized an acetone solution of permanganate immediately.

The mother liquors remaining after the isolation of the 2-benzoylbicyclo(1,2,2)heptene-2 were evaporated down; crystals with m. p. 65-70° (6.7 g) remained; they were dissolved in 15 ml of acetone with heating and left at room temperature. The material which crystallized out after 2-3 weeks (3.1 g, 20%) had m. p. 130-131°; after a second recrystallization from alcohol, the substance had m. p. 131-132°, λ_{max} 250 mμ; log ε 2.1 (in methanol); a mixture with 2-benzoylbicyclo(1,2,2)heptene-2 had m. p. 61-70°.

Found %: C 84.53, 84.83; H 7.21, 7.35. $C_{14}H_{14}O$. Calculated %: C 84.82; H 7.17.
The colorless prisms were difficultly soluble in ether, acetone, and alcohol and readily soluble in benzene and petroleum ether. They did not decolorize an acetone solution of permanganate.

2-p-Chlorobenzoylbicyclo(1,2,2)heptene-2 was synthesized by a method similar to that described in the previous experiment. From 0.70 g of 2-p-chlorobenzoyl-3-chlorobicyclo(1,2,2)heptane and 10 ml of triethylamine we obtained 0.53 g of a crystalline material with m. p. 65-70°. Recrystallization from ether at − 70° gave 0.36 g (60%) of material with m. p. 87.5-88.5°.

Found %: C 72.35, 72.41; H 5.85, 5.95. $C_{14}H_{13}OCl$. Calculated %: C 72.20; H 5.62.
The colorless crystals were soluble in ether, acetone and benzene. They decolorized and acetone solution of permanganate.

On partially evaporating the mother liquors, we obtained 0.5 g of a substance with m. p. 103-123°, which was not examined further. The substance did not decolorize an acetone solution of permanganate.

Found %: Cl 14.35. $C_{14}H_{13}OCl$. Calculated %: Cl 15.22.

Reactions of 2-Acylbicyclo(1,2,2)Heptenes-2

Reaction of 2-acetylbicyclo(1,2,2)heptene-2 with malonic ester. 12.0 g (0.075 mole) of malonic ester and 6.9 g (0.050 mole) of 2-acetylbicyclo(1,2,2)heptene-2 were added to a solution of sodium ethylate (from 0.1 g of sodium) in 25 ml of anhydrous ethanol. After 2-5 minutes, the reaction mixture heated up to 60-70°. When the evolution of heat ceased (30 minutes), the temperature of the mixture was kept at 50-60° for 6 hours, then the mixture was cooled and diluted with water, the precipitated oil extracted with ether and the extracts dried with sodium sulfate; after distilling off the solvent, the residue was distilled to give a fraction with b. p. 157-160° (2 mm); the yield was 11.7 g (78.6%), n_D^{20} 1.4720.

Literature data for 2-acetylbicyclo(1,2,2)heptyl-(3)-malonic ester [2]: b. p. 150-154° (1.5 mm) n_D^{20} 1.4714.

The colorless, viscous oil did not give a color with ferric chloride and did not decolorize an acetone solution of permanganate.

The 2,4-dinitrophenylhydrazone had m. p. 130-131° (from alcohol).

Reaction of 2-propionylbicyclo(1,2,2)heptene-2 with diethylamine. 7.0 g of 2-propionylbicyclo(1,2,2)-heptene-2 was dissolved in 20 ml of diethylamine and the solution boiled gently for 6 hours. Then the excess diethylamine was distilled off and the residue vacuum distilled to give a fraction with b. p. 89-90° (3 mm); the yield was 8.7 g (74.1%), n_D^{20} 1.4805, d_4^{20} 0.9440.

Literature data [3]: b. p. 98° (3 mm), n_D^{20} 1.4810, d_4^{20} 0.9441.

The hydrochloride of 2-propionyl-3-diethylaminobicyclo(1,2,2)heptane was prepared by saturating an ether solution of 1.3 g of the amine at −20° with dry hydrogen chloride; the yield was 1.47 g (97%), m. p. 141.5-142.5° (washed with ether on the filter).

Found %: Cl 13.80, 13.86. $C_{14}H_{26}ONCl$. Calculated %: Cl 13.65.

The methiodide was prepared as described previously [3]; m. p. 143-144°; a mixed melting point with an authentic sample [3] was not depressed.

Hydrogenation of 1.4 g of 2-benzoylbicyclo(1,2,2)heptene-2 was carried out in 20 ml of ether over 0.1 g of $Pd/BaSO_4$. 150 ml of hydrogen (0.0068 mole, 760 mm, 0°) was absorbed in 5 hours. After evaporating off the ether, the residue was vacuum distilled; yield 1.1 g.

B. p. 155-158° (10 mm), n_D^{20} 1.5540.

Found %: C 83.34, 83.21; H 7.96, 8.04. $C_{14}H_{16}O$. Calculated %: C 83.96; H 8.05.

The 2,4-dinitrophenylhydrazone of 2-benzoylbicyclo(1,2,2)heptane was prepared in alcohol; the orange tablets had m. p. 155-156° (from glacial acetic acid).

Found %: N 14.27, 4.22.* $C_{20}H_{20}O_4N_4$. Calculated %: N 14.73.

2-Benzoylbicyclo(1,2,2)heptene-5. 10.6 g (0.08 mole) of phenyl vinyl ketone was mixed with 13 g (0.20 mole) of cyclopentadiene. After 10-15 minutes, the mixture gave off heat strongly; by cooling it in water, the temperature was kept at about 50°. After the evolution of heat, the mixture was left overnight and distilled the following day to give a fraction with b. p. 135-136° (7 mm); the yield was 13.0 g (80%), n_D^{20} 1.5660.

Literature data [7]; b. p. 121-122° (3 mm), n_D^{26} 1.5648.

Hydrogenation of 9.0 g of 2-benzoylbicyclo(1,2,2)heptene-5 was carried out in 20 ml of ether over 0.1 g of palladium on barium sulfate. Over a period of 2 hours, 110 ml of hydrogen (0.0049 mole, 760 mm, 0°) was absorbed. After distilling off the solvent, we distilled the residue and collected a fraction with b. p. 157-159° (11 mm); the yield was 8.7 g (96.7%), n_D^{20} 1.5570.

The 2,4-dinitrophenylhydrazone had m. p. 155-156° (from glacial acetic acid); a mixed melting point with the sample obtained in the previous experiment was not depressed.

SUMMARY

1. We developed a general method for synthesizing 2-acylbicyclo(1,2,2)heptenes-2 by reacting 2-acyl-3-chlorobicyclo(1,2,2)heptanes with triethylamine.

2. It was shown that aryl β-chlorovinyl ketones, that are substituted in the nucleus, condense with cyclopentadiene like their aliphatic analogs.

3. It was shown that 2-acylbicyclo(1,2,2)heptenes-2 have an active double bond which adds nucleophilic reagents smoothly.

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CATALYTIC ALKYLATION OF PHENOL WITH ETHYL ALCOHOL

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The condensation of phenol with ethyl alcohol in the presence of $ZnCl_2$ [1] or $HClO_4$ [2] gave a small amount of phenol alkylation products and from this mixture o- and p-ethylphenols were isolated. Later [3] large yields were obtained by alkylating phenol with ethyl alcohol in the presence of aluminum chloride. 3,5-Diethylphenol, o-ethylphenol and, presumably, p-ethylphenol were isolated from the alkylphenol mixture obtained.

In this work we investigated the reaction of phenol with ethyl alcohol in the vapor phase over activated gumbrine, i.e., under the conditions used for the alkylation of phenol with methyl alcohol [4]. Phenol reacted with ethyl alcohol to give alkylated phenols (main product), neutral products and also gas and water. To find the optimal alkylation conditions we studied the effect of temperature, the ratio of the starting materials and rate of their passage over the catalyst on the reaction product yield.

The optimal temperature for phenol alkylation with ethyl alcohol is 350° (table). Increasing the temperature to 500° resulted in a considerable decrease in yield. The maximum amount of neutral oil was obtained at 250° and its yield decreased with an increase in temperature. The greatest yield of alkyl derivatives of phenol was obtained at a molar ratio of phenol and alcohol of 1:2. An increase in this ratio to 1:6 decreased their yield. With the same ratio of starting components the amount of alkali-insoluble neutral reaction products formed showed an inverse relationship: their yield increased with an increase in the amount of alcohol in the initial mixture. An increase in the rate of passage of the initial mixture over the catalyst affected the yield of alkylation products negatively. The greatest yield of the latter was obtained at the slowest rate.

Thus, the optimal conditions for phenol alkylation with ethyl alcohol are the following: a temperature of 350°, a molar ratio of phenol to alcohol of 1:2 and a flow rate of the initial mixture of 12 ml per hour (over 115 ml of catalyst). Under these conditions the yield of alkylated phenols was 61.8% (calculated on the condensate), or 94.4% (calculated on the initial phenol). The yield of neutral oils under these conditions was 2.67% (calculated on the condensate).

By fractionating the catalytic alkylation products we isolated and characterized the following individual phenols: o- and p-ethylphenols and 3,5- and 2,4-diethylphenols. The alkali-insoluble neutral products of the condensation of phenol with ethyl alcohol were obtained in very small amounts (2.67% calculated on the condensate) under the optimal conditions for alkylphenol yields. Fractionation of the neutral product on an analytical column gave a small amount of phenetole and ethylphenetole.

Under the optimal conditions for the formation of higher phenols, the gaseous products had the following composition: ethylene 99%, residue 1%.

In studying the reactions of phenol with alcohols in the presence of $AlCl_3$, I. P. Tsukervanik and Z. N. Nazarova [5] concluded that alkylation of phenol with alcohols proceeded through the intermediate formation of phenol ethers. Such an alkylation mechanism also seems very probable to us in the alkylation of phenol with ethyl alcohol on natural aluminosilicate catalyst investigated by us. We found a small amount of alkylphenol ethers in the neutral reaction products. Their small yield is possibly due to the fact that these ethers are obtained as intermediate substances. In order to check this hypothesis an experiment was carried out on the decomposition of ethyl phenyl ether under the same conditions as the experiments on the condensation of phenol with ethyl alcohol. The condensate obtained contained up to 60% of alkylated phenols. The gas thus

The Effect of Reaction Temperature on Alkylation of Phenol with Ethyl Alcohol (Molar ratio of phenol : alcohol = 1 : 6; flow rate of mixture 12 ml per hour; amount of catalyst 115 ml)

Yield (in %)	Temperature		
	250°	350°	500°
Condensate	61.2	63.83	56.6
Higher phenols (calc. on condensate)	12.66	37.05	34.25
Higher phenols (calc. on initial phenol)	30.52	93.09	76.3
Unchanged phenol in condensate	10.55	8.37	30.16
Neutral oil (calc. on condensate)	10.1	5.1	5.81

formed contained 75% of ethylene. In this way, the experimental data confirmed the possibility of alkyl phenyl ethers being converted into alkylated phenols under our conditions.

Alkylation of phenol with alcohol may proceed in the following directions:

$$\left.\begin{aligned} C_6H_5OH + C_2H_5OH &\longrightarrow C_6H_5OC_2H_5 + H_2O \\ C_6H_5OC_2H_5 &\longrightarrow C_6H_5OH + C_2H_4 \\ C_6H_5OH + C_2H_4 &\longrightarrow o\text{- \& } p\text{-}C_2H_5C_6H_4OH \end{aligned}\right\} \quad (I)$$

According to this scheme the phenetole formed decomposes to phenol and ethylene while the olefin liberated is the alkylating agent. We detected ethylene both in the main experiments on the condensation of phenol with ethyl alcohol and in the experiment with phenetole.

$$\left.\begin{aligned} C_6H_5OH + C_2H_5OH &\longrightarrow C_6H_5OC_2H_5 + H_2O \\ C_6H_5OC_2H_5 &\longrightarrow o\text{- \& } p\text{-}C_2H_5C_6H_4OH \end{aligned}\right\} \quad (II)$$

According to the second scheme, migration of the ethyl group into the ortho- and para-positions occurs.

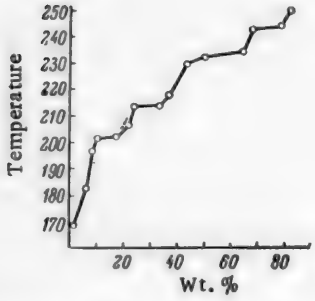
We find both schemes quite probable and it is possible that both processes occur simultaneously.

EXPERIMENTAL

The condensation of phenol with ethyl alcohol was performed in the apparatus normally used for vapor-phase catalytic investigations. A mixture of dry, freshly distilled phenol and 98% alcohol (rectified) in a molar ratio of 1 : 6 was passed through a reaction tube, filled with activated chloride and granulated gumbrine, at 350°, at a rate of 12 ml per hour for 115 ml of catalyst. (After passing 200 ml of the mixture, we placed a fresh portion of catalyst in the reaction tube.) From a total of 1720 g of the mixture of phenol and alcohol, we obtained 1154 g of a two-layer condensate. The weight of the aqueous layer was 520.5 g and that of the oily layer, 612.1 g. A product, boiling at up to 100°, was distilled off from the oily layer and added to the aqueous layer. After a preliminary extraction with ether, the aqueous layer distilled completely at 100-102°. The oily layer was combined with the ether extracts from the aqueous layer and treated several times with a 20% solution of NaOH. As a result we obtained 19.55 g of a neutral oil and 569.63 g of an alkali-soluble, phenolic product.

Analysis of phenols. The phenol derivatives were first distilled off from the unchanged starting phenol. 418.27 g of a fraction, boiling in the range 183-240°, was distilled on a fractionating column, 1.5 meters high, packed with glass, Fensky rings, with an efficiency of 40 theoretical plates. We obtained 15 fractions, shown on the distillation curve (figure).

The fraction 242.5-245° crystallized. The products, boiling in the ranges 201-202, 213.5-215 and 230-235° were further distilled on an analytical column with a nickel spiral (column height, 90 cm, diameter, 0.4 cm, efficiency, 25 theoretical plates). As a result of the distillation, we obtained fractions corresponding in boiling point to the following individual alkylphenols: o-ethylphenol, 3,5-diethylphenol, p-ethylphenol and 2,4-diethylphenol.



Distillation curve of the phenols on a column with an efficiency of 40 theoretical plates (p= 766.4 mm, amount of phenols, 418.27 g).

o-Ethylphenol: b.p. 202-203° (766.7 mm), d_4^{20} 1.0177, n_D^{20} 1.5363.

Found %: OH 14.0, 13.5. M 125.5, 123.5. $C_8H_{10}O$. Calculated %: OH 13.9. M 122.2. Melting point of o-ethylphenoxyacetic acid 140°.

p-Ethylphenol: b. p. 214-215° (766.7 mm), d_4^{20} 1.0097, n_D^{20} 1.5328.

Found %: C 78.81; H 8.72; OH 14.05. M 122.2. $C_8H_{10}O$. Calculated %: C 78.69; H 8.20; OH 14.05. M 122.2.

2,4-Diethylphenol: b. p. 229-230° (766.7 mm), d_4^{20} 0.9811, n_D^{20} 1.5264.

Found %: C 79.86; H 9.27; OH 11.27. M 147.2, 147.9. $C_{10}H_{14}O$. Calculated %: C 80.00; H 9.33; OH 11.33. M 150.

3,5-Diethylphenol: b. p. 242.5-245° (766.7 mm), m. p. 76-76.5° (needles from light benzine).

Found: M 147.3, 148. $C_{10}H_{14}O$. Calculated: M 150.

The tribromide, prepared by Jannasch's method [6] was recrystallized several times from glacial acetic acid and had m. p. 128-128.6°.

Analysis of neutral products. 19.5 g of the alkali-insoluble neutral reaction product was distilled on the analytical column. As a result of the fractionation, we isolated products with b. p. 170-171° and 193-194°. The product with b. p. 170-171° contained phenetole.

Found: M 126.1, 126.3. $C_8H_{10}O$. Calculated: M 122.2.

The fraction 193-194° contained ethylphenetole.

Found: M 154.1, 154.3. $C_{10}H_{14}O$. Calculated: M 150.0.

The presence of ethoxyl groups in the first and the second products was proved.

SUMMARY

1. Phenol reacts with ethyl alcohol in the vapor phase over an aluminosilicate catalyst (gumbrine clay) to form a mixture of alkylated phenols, ethylene and a small amount of neutral products. The mixture of alkylphenols yielded the following individual products: o- and p-ethylphenols and 2,4- and 3,5-diethylphenols.

2. Under optimal reaction conditions the yield of alkylphenols was 94.4% (calculated on the initial phenol).

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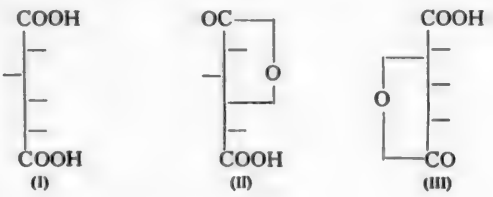
THE FORMATION AND HYDROLYSIS KINETICS OF MONOLACTONES OF D-GLUCOSACCHARIC AND D-TALOMUCIC ACIDS

L. Mai

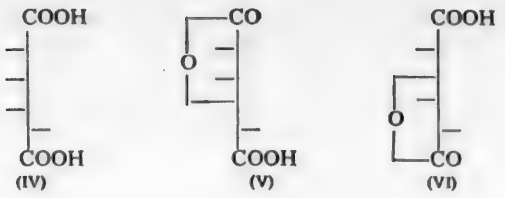
One of the most characteristic properties of polyhydroxy-dicarboxylic (saccharodicarboxylic) acids, namely their tendency to form lactones, depends to a large extent on the steric configuration of the polyhydroxymethylene chain. As far as we know, no systematic and quantitative investigation of this relation, which would be valuable for studying the acid-lactone equilibrium and for determining its steric factors, has as yet been carried out. E. Fischer noted the great differences in the rate of lactonization, the position of the acid-lactone equilibrium and the stability of the lactones of diastereoisomeric aldonic and, particularly, dicarboxylic acids from aldoses [1]. According to Hjelt's data the lactonization rate of D-glucosaccharic acid is considerably lower than that of mucic acid [2]. Levene and Simms state that the lactonization rate of all aldonic and saccharodicarboxylic acids is practically the same and does not depend on the solubility and ease of separation of the lactone [3]. Haworth et al., on the contrary, report a noticeable relation between the rates of lactonization and hydrolysis of methylated aldonic acid lactones to the configuration [4]. Lactone formation is controlled by the law of monomolecular reactions [3, 5]. The relation of the formation of γ - or δ -lactone of aldonic acids to steric factors was studied by Rehorst [6]. As is known, the kinetics of aldonolactone formation and hydrolysis are specific for the given type of lactone ring (γ - or δ -); kinetic analysis of aldonolactone hydrolysis has therefore become a valuable method for establishing the cyclic structure of sugars and their derivatives [4].

In this work we used polarimetric measurements to study the rates of formation and hydrolysis of the monolactones (II), (III), (V), (VI) of D-glucosaccharic (I) and D-talomucic (IV) acids. We chose these acids and their monolactones as, firstly, all of them may be prepared in a pure crystalline state. Secondly, only D-glucosaccharic and D-talomucic acids (and of course, the corresponding acids of the L series) of all the dicarboxylic acids from aldohexoses, form two diastereoisomeric monolactones each (one 1,4- and one 3,6-monolactone each); • due to their symmetrical (meso-) structure allomucic and mucic acids each form two enantiostereoisomeric monolactones, while mannosaccharic and idosaccharic acids may form theoretically only a single monolactone each; however, only dilactones of D- and L-mannosaccharic acids are known.

Meyer measured polarimetrically the rates at which the acid-lactone equilibrium was established for D-glucosaccharic acid and its 3,6-monolactones [5]; crystalline D-glucosaccharic acid was not known then and a solution of it was prepared by an indirect method (from the Ag-salt and hydrochloric acid). Steiger and Reichstein obtained polarimetric data for D- talomucic acid and its monolactones at various temperatures in the range 14-24° [7].



• Arabo-trihydroxyglutaric acid has a similiar position in the series of dicarboxylic acids from aldopentoses.



The measurement and storage temperature for the solutions in our experiments was 18 ± 2°. The measurements were carried out on a half-shadow apparatus with a triple band field of vision, which made it possible to read off 0.01°; the mean value of three readings was used for determining the angle of rotation. The tube was 2 dm long; $[\alpha]_D$ was calculated normally; c = 2.0000 for (I) and (IV), 8.1500 for (II) and (III) and 2.2221 for (V) and (VI) (it was established in preliminary experiments that the $[\alpha]_D$ for all the substances investigated depended to a very small degree on concentration). The time is given in hours, starting from the moment of complete solution of the substance. The value of α_t for t = 0 was extrapolated from the curves for (II), (IV), (V) and (VI); α_0 corresponded to t = 0.08 hours for (I) and (III). The rate constants K_1 and K_2 are given in [hours^{-1}] and are calculated from the equations (1, 2, 3) [5].

$$\frac{K_1}{K_2} = \frac{\alpha_L - \alpha}{\alpha - \alpha_A} \tag{1}$$

$$K_1 + K_2 = \frac{1}{t} \ln \frac{\alpha_L - \alpha}{\alpha_t - \alpha} \tag{2}$$

$$K_1 + K_2 = \frac{1}{t} \ln \frac{\alpha - \alpha_A}{\alpha - \alpha_t} \tag{3}$$

where K_1 is the rate constant of lactone hydrolysis, K_2 is the rate constant of acid lactonization, α_D is the specific rotation of the monolactone, α_A is the specific rotation of the acid, α is the specific rotation of the equilibrium mixture, α_t is the specific rotation at time t; equation (2) was used for acid hydrolysis, (3) was used for acid lactonization. Measurements were carried out for 70-75 days. The final measurement results are given in the table. The values for the sum $K_1 + K_2$ are the average of 7-9 measurements of α; the maximum difference of the separate magnitudes of this sum for D-glucosaccharic acid and its lactones was not greater than ± 0.004 and for D-talomucic acid and its lactones ± 0.0008. K_1 and K_2 were calculated from the average arithmetical sum of $K_1 + K_2$, obtained from equations (2) and (3).

Basic Data on the Kinetics of Formation and Hydrolysis of D-Glucosaccharic and D-Talomucic Monolactones

Starting material	α_0	α	$K_1 + K_2$	K_1	K_2	$\frac{K_1}{K_2}$
D-Glucosaccharic acid (I)	6.86	22.16	0.013	—	—	—
1,4-Monolactone (II)	32.90	22.50	0.010	0.0045	0.0070	0.665
3,6-Monolactone (III)	40.78	22.30	0.011	0.0065	0.0055	1.197
D-Talomucic acid (IV)	30.70	7.70	0.0042	—	—	—
1,4-Monolactone (V)	—49.90	8.02	0.0031	0.0022	0.0014	2.554
3,6-Monolactone (VI)	33.80	8.40	0.0030	0.0019	0.0017	1.139

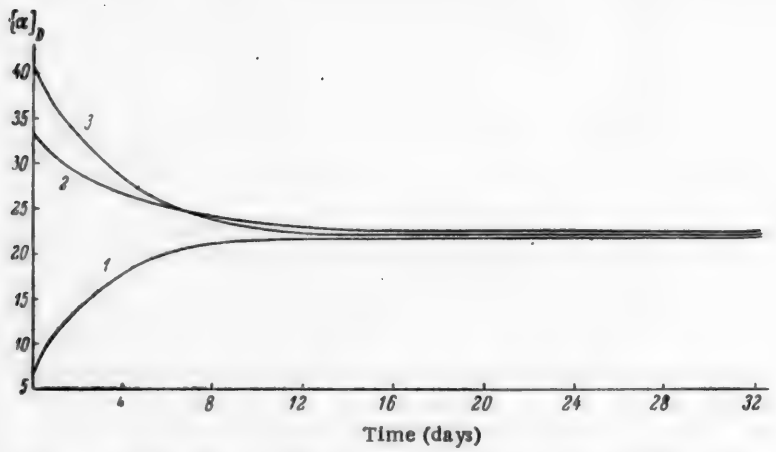


Fig. 1. The formation and hydrolysis curves of D-glucosaccharic monolactones. 1) D-glucosaccharic acid; 2) 1,4-monolactone; 3) 3,6-monolactone.

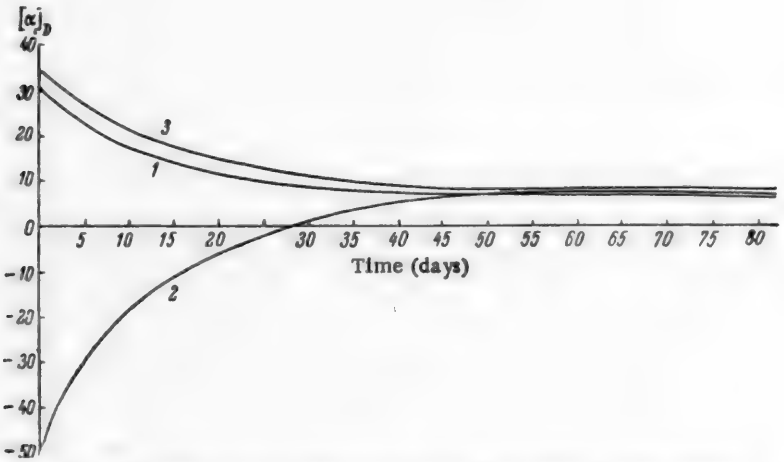


Fig. 2. The formation and hydrolysis curves of D-talomucic monolactones. 1) D-talomucic acid; 2) 1,4-monolactone; 3) 3,6-monolactone.

The course of lactonization and hydrolysis is illustrated graphically in Figs. 1 and 2.

Meyer [5] gave the following rate constants for D-glucosaccharic acid and its 3,6-monolactone: for 18° $K_1 = 0.00559$, $K_2 = 0.00385$ (starting from the lactone) $K_1 = 0.00567$, $K_2 = 0.00394$ (starting from the acid); and for 25.2°, $K_1 = 0.01176$, $K_2 = 0.00891$ (starting from the lactone) $K_1 = 0.01168$, $K_2 = 0.00879$ (starting from the acid), which agree quite well with our data if one considers the possible errors in calculating large time periods.

It took about 20 days to establish the acid-monolactone equilibrium for D-glucosaccharic acid and about 60 days for D-talomucic acid. The hydrolysis rate constants of the diastereoisomeric D-glucosaccharic mono-

lactones differed little among themselves but were noticeably greater than the hydrolysis rate constants of the diastereoisomeric D-talomucic monolactones. Approximately the same ratio exists between the lactonization rate constants of D-glucosaccharic and D-talomucic acids. The hydrolysis kinetics of saccharodicarboxylic monolactones are thus not specific for the given steric configuration, at least not in the cases investigated.

The only reliable criteria of the tendency of saccharodicarboxylic acids to lactonize is, apparently, the composition of the acid-lactone equilibrium mixture and the amount of monolactones characteristic of the given sugar chain.

SUMMARY

1. The formation and hydrolysis rate constants were determined polarometrically for 1,4- and 3,6-monolactones of D-glucosaccharic and D-talomucic acids.

2. The two diastereoisomeric monolactones of a saccharodicarboxylic acid have practically the same hydrolysis rate.

3. The lactonization rate of D-glucosaccharic acid and the hydrolysis rate of its monolactones are considerably greater than those of D-talomucic acid.

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THE REACTION OF ETHERS WITH ANILINE AND AMMONIA

II. REACTION OF ANISOLE WITH ANILINE

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In spite of great theoretical interest, the reaction of mixed ethers with amines has not been studied up to now. Only the reaction of anisole with ammonia is described in the literature. Chatterjee, Sanyal and Goswami [1] reported the formation of amines by passing anisole and ammonia vapor over dehydrating catalysts. Lately, Kozlov and Akhmetshina [2] showed that a catalytic reaction of anisole with ammonia over active aluminum oxide at 450-475° and a pressure of 8-9 atm gave mainly aniline and p-toluidine. Besides the amines, phenol and p-cresol were isolated from the catalyzate.

This report gives the experimental results of reacting aniline and anisole vapor over an aluminosilicate catalyst and over active aluminum oxide [3]. In order to find the most probable direction for the process, as the literature has no data on the character of the reaction of anisole and aniline, we carried out a preliminary thermodynamic calculation and computed the equilibrium constants of some reactions.

$$C_6H_5OCH_3 + C_6H_5NH_2 \rightleftarrows C_6H_5NHCH_3 + C_6H_5OH \quad (I)$$
$$C_6H_5OCH_3 + C_6H_5NHCH_3 \rightleftarrows C_6H_5N(CH_3)_2 + C_6H_5OH \quad (II)$$
$$C_6H_5OCH_3 + C_6H_5NH_2 \rightleftarrows C_6H_5NHC_6H_5 + CH_3OH \quad (III)$$

The calculations were analogous to those described earlier [3]. The calculation results are given in Table 1.

TABLE 1

Reaction No.	Temperature							
	200°		250°		300°		350°	
	K_p	yield %	K_p	yield %	K_p	yield %	K_p	yield %
(I)	3950	98.50	2140	97.90	1320	97.40	891	96.90
(II)	5760	98.75	2758	98.40	1562	97.50	1048	97.20
(III)	251	94.0	175	93.1	130	92.0	100	91.0

The yield was calculated for an equimolecular mixture. As the data given show, the reaction of anisole with aniline may proceed as alkylation of the amine (I) and (II) and as arylation of the amine (III). At the same time equilibrium conditions are more favorable for the reactions to proceed with the rupture of the CH_3-O bond in the anisole molecule.

Passing anisole and aniline vapor (molar ratio of 2:1) over active aluminum oxide at 200° gave a catalyzate containing considerable amounts of phenol, monomethylaniline and dimethylaniline, besides unreacted aniline and anisole. The catalyzate contained no other products in large amounts. The amount of phenol fully

corresponded to the amount of mono- and dimethylaniline and may be calculated from the catalyzate content of the latter by equations of reactions (I) and (II). This showed that at relatively low temperatures, of the order of 200°, in the reaction of anisole with aniline only alkylation of aniline with the anisole methyl group occurred.

On further raising the temperature (250-350°) the catalyzate compositions became more complicated. Besides the above substances, the catalyzate yielded o-, m- and p-cresols, xylenols and a certain amount of tar, which was not investigated further. Figure 1 shows graphically the change in the molar composition of the catalyzate with temperature. As the temperature increased, anisole content of the catalyzate fell continuously and in the temperature range (200-350°) the amount of aniline passed through a minimum at 250°, while the methyl- and dimethylaniline contents passed through a maximum (also at 250°); under these conditions, in all cases more methylaniline was formed than dimethylaniline. The phenol content of the catalyzate passed through a maximum (250°) with rising temperature while the amount of cresols increased continuously.

Figure 2 shows the relation of the molar composition of the catalyzate, obtained over aluminum oxide, to contact time at 300°. An increase in contact time was analogous in many ways to an increase in temperature. The amount of anisole continued to fall with increasing contact time. The amount of methyl- and dimethylaniline passed through a maximum and that of aniline through a minimum. The phenol content passed through a maximum and the amount of cresols increased continuously with increase in contact time. The course of the curves given in Figs. 1 and 2 show conclusively that with an increase in temperature, secondary processes start to occur, and these consist of the demethylation of the aliphatic-aromatic amines formed by reactions (I) and (II) while the nucleus of the phenol formed is methylated simultaneously by the reactions

$$C_6H_5NHCH_3 + C_6H_5OH \longrightarrow C_6H_5NH_2 + o\text{-, m- and p-}CH_3C_6H_4OH \quad (IV)$$

$$C_6H_5N(CH_3)_2 + C_6H_5OH \longrightarrow C_6H_5NHCH_3 + o\text{-, m- and p-}CH_3C_6H_4OH \quad (V)$$

The same rules were noticed in reacting anisole and aniline over synthetic aluminosilicate as over active aluminum oxide (Fig. 3). The methyl-, dimethylaniline and phenol content of the catalyzate passed through a maximum and that of aniline through a minimum (300°). The amount of anisole decreased continuously and that of cresol increased gradually with temperature. In contrast to the reaction on aluminum oxide, p-toluidine was formed on an aluminosilicate catalyst. As Fig. 3 shows, the p-toluidine content of the catalyzate increased continuously with rising temperature. The formation of some tar was also observed on an aluminosilicate catalyst.

In order to confirm the possibility of reactions (IV) and (V) proceeding under the conditions of aniline alkylation with anisole, we carried out experiments of phenol alkylation with methyl- and dimethylaniline on active aluminum oxide and synthetic aluminosilicate at 350°. From the catalyzate obtained over active aluminum oxide we isolated aniline, methyl- and dimethylaniline and o-, m- and p-cresols as well as a small amount of tar. Under the same conditions but on synthetic aluminosilicate, in addition to the above products, we obtained p-toluidine, N-monomethyl- and N-dimethyltoluidine and xylidines as well as some products with more highly alkylated nuclei (Table 2). The experiments carried out show that dealkylation of alkylanilines with phenols proceeded at a high rate at temperatures above 250-300°.

The reaction of anisole and aniline at high temperatures probably includes more reactions than (I), (II), (IV) and (V). At high cresol contents, the alkylation of cresols is also possible with aliphatic-aromatic amines by schemes analogous to (IV) and (V). Besides that, it is known [4] that in the presence of the catalysts investigated and in the same temperature range, anisole itself undergoes isomerization and disproportionation with the formation of phenol, cresols and xylenols. The ratio of the rates of the various reactions in the reaction of anisole and aniline depends on temperature and ratio of initial components and is being investigated further.

The facility with which the alkylation process occurs and the absence of diphenylamine in the catalyzate indicated that in reacting anisole and aniline at 200-350° only the $O\text{-}CH_3$ bond was broken, while under the given conditions the $C_6H_5\text{-}O$ bond remained whole and no aniline arylation (III) took place. This reaction, apparently, is possible only at higher temperatures.

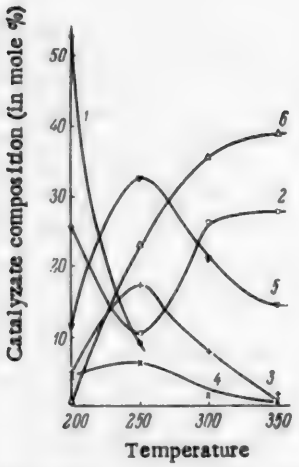

Fig. 1. The effect of temperature on catalyzate composition in reacting anisole and aniline on active aluminum oxide. 1) Anisole; 2) aniline; 3) methylaniline; 4) dimethylaniline; 5) phenol; 6) cresols.

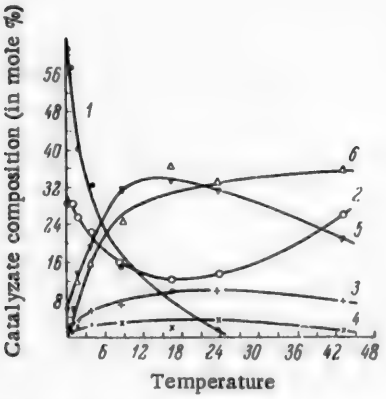

Fig. 2. The effect of contact time on catalyzate composition in reacting anisole and aniline on active aluminum oxide at 300°. 1) Anisole; 2) aniline; 3) methylaniline; 4) dimethylaniline; 5) phenol; 6) cresols.

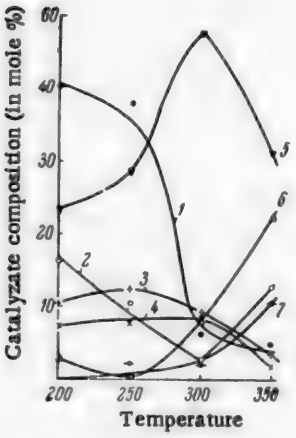

Fig. 3. The effect of temperature on catalyzate composition in reacting anisole and aniline on synthetic aluminosilicate. 1) Anisole; 2) aniline; 3) methylaniline; 4) dimethylaniline; 5) phenol; 6) cresols; 7) p-toluidine.

EXPERIMENTAL

The catalytic reaction of anisole and aniline was carried out in a flow system. After each experiment, the catalyst was regenerated in a stream of air at 500°. In these experiments, the anisole was first distilled off from the catalyzate on a column with an efficiency of 20 theoretical plates and then the amines and phenols were separated from the catalyzate by the usual methods. The amines obtained using an activated aluminum oxide catalyst were analyzed for aniline, methyl- and dimethylaniline content using Nelyubina's method [5]. The amines contained p-toluidine and a small amount of higher alkylated amines besides aniline and methyl- and dimethylaniline. The p-toluidine in this mixture was determined by precipitating the primary amines as the complex salts with cadmium chloride [6] and then titrating the aniline and p-toluidine isolated by the bromide – bromate method. The phenols were analyzed colorimetrically [7].

In experiments on the reaction of methylaniline and dimethylaniline with phenol, the amines and phenols were vacuum distilled after the preliminary separation and each fraction was analyzed separately by the methods given above.

In the catalytic reaction of anisole and aniline in the range 200-350°, no significant amounts of gaseous products were formed.

TABLE 2

Catalyst	Contact time (in sec)	Passed (in g)			Catalyzate formed (g)	Catalyzate composition (in g)									
		methylaniline	dimethylaniline	phenol		aniline	methylaniline	dimethylaniline	p-toluidine	monomethyl-p-toluidine	dimethyl-p-toluidine	xylidines	highly alkylated neutral substances	phenol	o-cresol	m-, p-cresols	highly alkylated phenols
Active aluminum oxide	41.4	151.1	—	130	278.4	55.5	40.5	6.6	—	—	—	—	8.57	55.0	38.9	16.0	10.1
Synthetic aluminosilicate	39.5	184.0	—	155	333.0	65.6	16.1	2.2	18.1	1.8	0.6	5.6	7.26	61.2	41.2	29.1	9.5
Active aluminum oxide	44.25	—	26.56	20.60	41.37	5.79	6.84	7.33	—	—	—	—	1.66	5.29	10.15*	—	0.67

* Total o-, m- and p-cresols.

In the experiments the following compounds were isolated and identified: aniline in the form of acetanilide, m. p. 113-113.5°; methylaniline in the form of N-methylbenzenesulfanilide, m. p. 79.0-79.5°; dimethylaniline in the form of the picrate, m. p. 161°; p-toluidine in the form of the acetyl derivative, m. p. 147.5° – 148.5°; phenol in the form of phenoxyacetic acid, m. p. 97.5-98°; o-cresol in the form of o-cresoxyacetic acid, m. p. 151.0 – 152.5°; m- and p-cresols in the form of the corresponding cresoxyacetic acids. The melting points of mixtures with authentic derivatives were not depressed.

SUMMARY

1. The reaction of anisole and aniline on active aluminum oxide and synthetic aluminosilicate was studied for the first time.

2. At 200-350° on these catalysts, rupture of the CH_3-O bond in an anisole molecule occurs accompanied by alkylation. The C_6H_5-O bond does not break under these conditions and no aniline arylation takes place.

3. The character of the alkylation depends on the nature of the catalyst. On active aluminum oxide, alkylation of aniline at the amino group and of phenol in the nucleus occurs. On synthetic aluminosilicate, alkylation of the aniline nucleus also occurs, besides the above processes.

4. For the first time methylaniline and dimethylaniline were dealkylated with phenol in the vapor phase.

5. Reaction schemes explaining the interaction of anisole and aniline are given.

6. The results of thermodynamic calculations on the anisole–aniline reaction are given.

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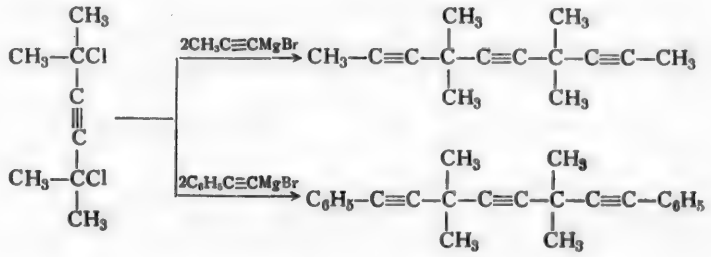
SYNTHESIS OF BRANCHED TRIACETYLENE HYDROCARBONS

II. PREPARATION OF 4,4,7,7-TETRAMETHYLDECATRIYNE-2,5,8 AND 3,3,6,6-TETRAMETHYL-1,8-DIPHENYL-OCTATRIYNE-1,4,7

A. I. Zakharova and G. D. Ilyina

In a previous paper [1] we proposed a method for preparing triacetylene hydrocarbons with triple bonds in the β-position by propargylation of alkyne-1-yl-magnesium bromides with tertiary acetylene dichlorides of the structure $R_2CCl-C\equiv C-CClR_2$. This method gave the first example of a fully methylated β-triyne with four quaternary carbon atoms – 2,2,5,5,8,8,11,11-octamethyl-dodecatriyne-3,6,9. A full summary of the literature on triacetylene synthesis was also given in the above paper. The only addition to this summary since then is a paper [2] on the synthesis of a triacetylene of normal structure with the triple bonds in the β-position – hexadecatriyne-5,8,11, carried out by two methods: the reaction of nonadiyne-1,4-ylmagnesium bromide with 1-bromoheptyne-2 and the reaction of two molecules of hexynylmagnesium bromide with 1,4-dibromobutyne-2. In addition, the same authors mention in another paper [3] the formation of dodecatriyne-1,4,7 as a side product in the synthesis of nonadiyne-1,4.

Continuing the investigation of the synthesis and properties of branched triacetylenes, we describe in this paper the preparation of two new examples of this class of compounds: 4,4,7,7-tetramethyldecatriyne-2,5,8 (I) and 3,3,6,6-tetramethyl-1,8-diphenyloctatriyne-1,4,7 (II). Hydrocarbon (I) was prepared by reacting 2,5-dichloro-2,5-dimethylhexyne-3 with methylacetylenylmagnesium bromide in the presence of Cu_2Cl_2 and $HgCl_2$ and hydrocarbon (II) by reacting the same acetylene dichloride with phenylacetylenylmagnesium bromide in the presence of the same catalysts.



The structure of the hydrocarbons was proved conclusively by ozonization. Decomposition of the ozonolysis products of hydrocarbon (I) gave dimethylmalonic and acetic acids. Trimethylmalonic and benzoic acids were found in the ozonolysis products of hydrocarbon (II). The existence of three triple bonds in hydrocarbon (I) was also proved by hydrogenating it in the presence of the catalyst $PdCl_2$ on $CaCO_3$. The theoretical amount of hydrogen required for converting hydrocarbon (I) to a saturated compound was absorbed.

EXPERIMENTAL

Preparation of 4,4,7,7-tetramethyl-decatriyne-2,5,8 (I). With continuous stirring and cooling, 45 liters of methylacetylene • was slowly passed (over a period of 40-45 hours) into the Grignard reagent prepared from 24 g of magnesium and 124 g of ethyl bromide in 700 ml of ether. Then the reaction mixture was heated on a water bath (bath temperature 30-35°) until the evolution of ethane ceased. With cooling, 2 g of freshly prepared cuprous chloride and 1 g of sublimed mercuric chloride were added to the methylacetylenylmagnesium bromide complex obtained, as catalyst, and then the acetylene dichloride (2,5-dichloro-2,5-dimethylhexyne-3• •) was introduced dropwise. The reaction mixture was stirred at room temperature for 3 days, boiled gently on a water bath for 6 hours and then decomposed with dilute hydrochloric acid after cooling. The separated ether solution was combined with ether extracts and dried over baked sodium sulfate and the ether distilled off. Distillation of the reaction products in vacuum yielded two fractions – the unreacted dichloride distilled off at up to 82° at 15 mm and the residual part distilled over at 5 mm and had b. p. 62-72°. The second fraction was distilled twice at 3 mm; we obtained a substance with b. p. 57-61°, which crystallized on standing in the cold. The hydrocarbon melted at 29° and formed white, feathery crystals. The yield was 45%.

Found %: C 90.24, 90.22; H 9.88, 10.02. M 186.3, 189. $C_{14}H_{18}$. Calculated %: C 90.32; H 9.68. M 186.2.

Ozonization of hydrocarbon (I). 5 g of hydrocarbon was ozonized in 30 ml of chloroform (until absorption of ozone ceased). The solvent was distilled off in vacuum; the ozonide was decomposed with water first at normal temperature and then with heating on a water bath. The ozonization products were treated with sodium bicarbonate and steam distilled and this gave no neutral products. The residual solution was acidified with sulfuric acid and on distillation, acetic acid was found among the volatile acids by the reaction with ferric chloride [6]. The residue from the distillation of the volatile acids was extracted with ether. On standing, the ether solution deposited crystals of dimethylmalonic acid with m. p. 189°. A mixed melting point with authentic dimethylmalonic acid was not depressed (m. p. 189-190°).

Preparation of 3,3,6,6-tetramethyl-1,8-diphenyl-octatriyne-1,4,7 (II). With continuous stirring, 69 g of phenylacetylene was added dropwise to a solution of Grignard reagent from 17 g of magnesium and 117 g of ethyl bromide in 600 ml of ether at such a rate that the ether in the flask boiled gently. Then the reaction mixture was heated on a water bath for several hours until ethylene was no longer evolved. 2 g of freshly prepared cuprous chloride and 1 g of mercuric chloride were added to the phenylacetylenylmagnesium bromide complex obtained, as catalyst, and then 60 g of acetylene dichloride (2, 5-dichloro-2,5-dimethylhexyne-3) was added dropwise. The reaction mixture heated up slightly. The next day stirring was continued at 35° for 8 hours and then the mixture was left at room temperature for a day. The complex was cooled in ice water and decomposed with a saturated solution of NH_4Cl (200 ml) and then dilute hydrochloric acid. The ether solution was washed with water and dried with baked sodium sulfate. After the ether and unreacted dichloride (in vacuum) had been distilled off, the residue crystallized. After two recrystallizations from a mixture of benzine and petroleum ether, the hydrocarbon had m. p. 142.5-143.5°. The yield was 35%.

Found %: C 92.63; H 7.41. M 311.2, 310.4 (Rast). $C_{24}H_{22}$. Calculated %: C 92.9; H 7.09. M 310.15.

Ozonization of hydrocarbon (II). 2.4 g of the hydrocarbon was ozonized in 50 ml of chloroform until the theoretical amount of ozone for 3 triple bonds (1.11 g of O_3) had been absorbed. The solvent was distilled off in vacuum and the ozonization product decomposed first with cold water and then with heating. There were no neutral products on steam distilling the ozonolysis products after treatment with sodium bicarbonate. Benzoic and dimethylmalonic acids were found among the acid products. The benzoic acid steam distilled and was sublimed. The m. p. was 121°. A mixed melting point with authentic benzoic acid was not depressed. After removal of the benzoic acid, the residue was extracted with ether. On standing, the ether solution deposited crystals of dimethylmalonic acid, which did not depress the melting point of authentic dimethylmalonic acid.

•For the preparation of methylacetylene see [4] (second method).

• •For the preparation of the dichloride see [5].

SUMMARY

1. By propargylating alkyne-1-ylmagnesium bromide with a tertiary acetylene dichloride of the structure $R_2CCl-C\equiv C-CClR_2$, we synthesized two new examples of branched triacetylene hydrocarbons with triple bonds in the β-position: a) 4,4,7,7-tetramethyl-decatriyne-2,5,8, by reacting methylacetylenylmagnesium bromide with 2,5-dichloride-2,5-dimethylhexyne-3, and b) 3,3,6,6-tetramethyl-1,8-diphenyloctatriyne-1,4,7 by reacting the above dichloride with phenylacetylenylmagnesium bromide.

2. The structure of the hydrocarbons was proved by ozonization to acetic and dimethylmalonic acids and benzoic and dimethylmalonic acids, respectively.

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SYNTHESIS OF p-, o- AND m-NITROETHYLBENZENES

P. M. Kochergin

The industrial use of p-, o- and m-nitroethylbenzenes necessitated this investigation for determining the physicochemical constants of mononitroethylbenzenes more accurately.

A series of authors [1, 2] have shown that nitration of ethyl benzene with nitrating mixture gives a mixture of p-, o- and m-nitroethylbenzenes. These compounds have very close boiling points* and fractional distillation of a mixture of mononitroethylbenzenes to obtain individual compounds presents certain difficulties. Thus, for example, Beilstein and Kuhlberg [3] obtained p- and o-nitroethylbenzenes with constant boiling points after 20 fractional distillations of the mononitroethylbenzene mixture at atmospheric pressure, and Schultz and Fläschslander [1] – after 80 distillations in vacuum followed by 100 distillations at atmospheric pressure. It should be noted that it is doubtful whether the above authors actually did have p- and o-nitroethylbenzene in a pure state. According to data in [1], p-nitroethylbenzene has m. p. –32° and o-nitroethylbenzene has m. p. –23°, while Birch et al. [5] obtained p-nitroethylbenzene with a m. p. –12.3°. These authors report that the given melting point corresponded to a 98.4% para-isomer content, but did not indicate the melting point of pure p-nitroethylbenzene. There is no information on the melting point of m-nitroethylbenzene in the literature. The literature contains rather contradictory data on the other physical constants of mononitroethylbenzenes – boiling points, specific gravities and refractive indices.

We synthesized p-, o- and m-nitroethylbenzenes by a method which excluded the presence of isomeric nitro compounds; p- and o-nitroethylbenzenes were prepared by the following scheme:

$$C_2H_5C_6H_4NO_2 \rightarrow C_2H_5C_6H_4NH_2 \rightarrow C_2H_5C_6H_4NH_2 \cdot {}^1/_2H_2SO_4 \rightarrow$$
$$\rightarrow C_2H_5C_6H_4N_2SO_3H \rightarrow C_2H_5C_6H_4NO_2$$

The mixture of mononitroethylbenzenes, prepared by nitration of ethylbenzene using the method described by Nelson and Brown [6] for nitration of tert-butylbenzene, was fractionally distilled in vacuum on a bubble-cap column. The technical p- and o-nitroethylbenzenes isolated were reduced with hydrogen in the presence of Raney nickel. The p- and o-aminoethylbenzenes obtained were converted into sulfates. The p-aminoethylbenzene sulfate was purified to constant melting point (238-239°) by recrystallization from water [7]; in contrast to o- and m-aminoethylbenzene sulfates, this sulfate was difficultly soluble in cold water. The o-aminoethylbenzene sulfate was purified to constant melting point (158-159°) by recrystallization from alcohol. The chemically pure p- and o-aminoethylbenzene sulfates were diazotized with sodium nitrite in dilute sulfuric acid and then the diazo group was substituted by the nitro group by Sandmeyer's reaction. The p- and o-nitroethylbenzenes obtained were isolated by steam distillation of the reaction mixture, extraction from the distillate with an organic solvent and purification by several distillations in vacuum to constant solidification points.

It was established that n-nitroethylbenzene had a solidification point of –11.5° and o-nitroethylbenzene –11°.

m-Nitroethylbenzene was obtained by the scheme:

* p-Nitroethylbenzene – b. p. 241-242° [1], 245-246° [3], 126° (13 mm) [2]; o-nitroethylbenzene – b. p. 223-224° [1], 227-228° [3], 109° (13 mm) [2]; m-nitroethylbenzene – b. p. 242-243° [4], 115.5° (13 mm) [2].

$$CH_3COC_6H_4NO_2 \rightarrow CH_3COC_6H_4NH_2 \rightarrow C_2H_5C_6H_4NH_2 \rightarrow$$
$$\rightarrow C_2H_5C_6H_4N_2SO_3H \rightarrow C_2H_5C_6H_4NO_2$$

m-Aminoacetophenone was prepared by reducing m-nitroacetophenone with hydrogen in the presence of Raney nickel. It was then treated with hydrazine hydrate in the presence of potassium hydroxide in diethyleneglycol by Kischner's reaction to give m-aminoethylbenzene. Diazotization of the amine followed by substitution of the diazo group by the nitro group, as in the case of p- and o-isomers, gave m-nitroethylbenzene with a solidification point of −37.9°.

The immediate starting substances, p-, o- and m-aminoethylbenzenes, for the synthesis of p-, o- and m-nitroethylbenzenes were characterized as the sulfates, hydrochlorides and picrates. It was found that o-aminoethylbenzene hydrochloride has m. p. 204-205° and not 191° [8], or 172-173° [9], as reported in the literature; the o-aminoethylbenzene picrate has a melting point of 147-148° and not 194-195° [7].

I would like to express my thanks to A. M. Grigorovsky for his constant attention and valuable advice during this work.

EXPERIMENTAL

p-Aminoethylbenzene (I). 370 g of p-nitroethylbenzene (n_D^{20} 1.5451) in 280 ml of alcohol was reduced with hydrogen in the presence of 11 g of moist Raney nickel. The reaction was carried out in an autoclave at 70-85° and with an initial hydrogen pressure of 100 atm. The reduction proceeded very rapidly. When the absorption of hydrogen ceased, the solution was cooled, filtered free from catalyst and diluted with acetone (1.5 liters). With cooling and stirring, 135 g of 92% sulfuric acid was added to the solution; the precipitate was filtered off, washed with acetone and then ether and dried. We obtained 310 g (74.5%) of a substance with m. p. 235-237°; after recrystallization from water, 171 g of p-aminoethylbenzene sulfate with m. p. 238-239° was isolated. The salt was difficultly soluble in cold water and methyl and ethyl alcohols. It crystallized from water in the form of colorless plates and from the lower alcohols in the form of colorless prisms.

By decomposition of a small amount of the pure sulfate with an aqueous solution of sodium bicarbonate, extraction of the base with ether, subsequent evaporation of the solvent and vacuum distillation of the material, we isolated p-aminoethylbenzene with b. p. 95-96° (10 mm).

The picrate formed long, curved needles or prisms (from dichloroethane) with m. p. 171-172° (with decomp.); it was readily soluble in alcohol and acetone and difficultly soluble in water and dichloroethane.

Found %: * N 16.11. $C_{14}H_{14}O_7N_4$. Calculated %: N 15.99.

The hydrochloride formed colorless, truncated prisms (from dichloroethane) with m. p. 199-200°; it was readily soluble in water, acetone, alcohol and chloroform and difficultly soluble in dichloroethane and ethyl acetate.

Found %: Cl 22.83. $C_8H_{12}NCl$. Calculated %: Cl 22.49.

o-Aminoethylbenzene (II). 311 g of o-nitroethylbenzene (n_D^{20} 1.5363) in 310 ml of alcohol was reduced with hydrogen in the presence of 10 g of moist Raney nickel, as in the preparation of (I). After distilling off the alcohol, we vacuum distilled the residual base. We obtained 220 g (88.3%) of o-aminoethylbenzene with b. p. 94-96° (10 mm). With cooling and stirring, 92 g of 93.5% sulfuric acid was added to 218 g of the amine in 800 ml of ether; the precipitate was filtered off, washed with ether and dried. We obtained 303 g of a substance with m. p. 155-156°; after 3 recrystallizations from alcohol, 209 g of o-aminoethylbenzene sulfate with m. p. 158-159° was isolated. The salt was readily soluble in water, methanol and ethanol and difficultly soluble in chloroform, ethylacetate and dichloroethane; it crystallized from water, methanol and ethanol as colorless prisms.

*All the analyses were carried out in the microanalysis laboratory of our institute, directed by V. V. Kolpakova.

Found %: S 9.61. $C_{16}H_{24}O_4N_2S$. Calculated %: S 9.42.

By decomposition of the pure sulfate with sodium bicarbonate as in the case of (I), we obtained o-aminoethylbenzene with b. p. 94-95° (10 mm).

The picrate formed yellow, rhombic plates (from dichloroethane) with m. p. 147-148°; it was readily soluble in the lower alcohols and acetone and difficultly soluble in dichloroethane and water; it crystallized from water in the form of yellow prisms. A mixture with the picrate of (I) (m. p. 171-172°) melted at 131-133°.

Found %: N 16.14. $C_{14}H_{14}O_7N_4$. Calculated %: N 15.99.

The hydrochloride formed colorless needles (from anhydrous acetone) with m. p. 204-205°; it was readily soluble in water, the lower alcohols and acetone and difficultly soluble in anhydrous acetone. A mixture with the hydrochloride of (I) (m. p. 199-200°) melted at 125-128°

Found %: Cl 22.59. $C_8H_{12}NCl$. Calculated %: Cl 22.49.

m-Aminoethylbenzene (III). A mixture of 70 g of m-aminoacetophenone (m. p. 97-97.5°), 100 g of potassium hydroxide, 70 ml of 85% hydrazine hydrate and 450 ml of diethylene glycol was heated in a flask with a reflux condenser and then a Dean and Starke apparatus, under the conditions described by Baker et al., [10]. After two vacuum distillations, we obtained 45 g (71.7%) of m-aminoethylbenzene as a colorless oil with b. p. 100-101° (14.5 mm).

The picrate formed yellow prisms (from dichloroethane) with m. p. 168-169° (with decomp.); it was readily soluble in alcohols, acetone and ethyl acetate, difficultly soluble in dichloroethane, water and glacial acetic acid and almost insoluble in chloroform. A mixture with the picrate of (I) (m. p. 171-172°) melted at 152-156°. A mixture with the picrate of (II) (m. p. 147-148°) melted at 134-138°.

Found %: N 16.16. $C_{14}H_{14}O_7N_4$. Calculated %: N 15.99.

The hydrochloride formed colorless, cubic crystals (from dichloroethane) with m. p. 159-160°; it was readily soluble in water, alcohol, acetone and chloroform, difficultly soluble in dichloroethane and almost insoluble in carbon tetrachloride. A mixture with the hydrochloride of (I) (m. p. 199-200°) melted at 134-137°. A mixture with the hydrochloride of (II) (m. p. 204-205°) melted at 120-124°.

Found %: Cl 22.58. $C_8H_{12}NCl$. Calculated %: Cl 22.49.

The sulfate formed colorless, elongated plates (from anhydrous chloroform), which were extremely hygroscopic in air; it was readily soluble in water, alcohol and acetone and difficultly soluble in chloroform, dichloroethane, toluene and tetrachloride.

p-Nitroethylbenzene (IV). With stirring, a solution of 66 g of sodium nitrite in 100 ml of water was added over a period of 30 minutes to a suspension of 164 g of the sulfate of (I) (m. p. 238-239°) in 600 ml of 15% sulfuric acid. The temperature of the reaction mixture was kept at from −4 to −8° by external cooling and also by the addition of a small amount of ice to the reaction mixture. At the end of the reaction, the diazo solution was neutralized at the same temperature with a 20% solution of sodium hydroxide (about 160 ml) to a pH of about 4 (indicator – bromophenol blue). With stirring and cooling to −8 to −10°, the solution obtained was gradually added over a period of 5-7 minutes to a suspension of 495 g of sodium nitrite and 41 g of cupricuprosulfite in 600 ml of water, when there was a vigorous evolution of nitrogen and considerable tar formation. At the end of the addition, the mixture was stirred and cooled for 1 hour and then steam distilled after standing at room temperature overnight. A small amount of nitrogen oxides was liberated during the distillation. The distillate was neutralized with excess sodium carbonate solution and extracted with chloroform. After drying the extract with calcium chloride, we evaporated off the solvent and vacuum distilled the residual oily material. We obtained 31.1 g (22.3%) of p-nitroethylbenzene; after 5 vacuum distillations, in which the middle fraction was distilled each time, we isolated 19.6 g of pure p-nitroethylbenzene. The clear, light yellow liquid had b. p. 92-93° (2 mm), 248-249° (752 mm), solidification temperature −11.5°,* n_D^{20} 1.5460, d_4^{20} 1.1226.

* The determination of the solidification temperatures, refractive indices and specific gravities of the nitroethylbenzenes was carried out in the analytical control laboratory of our institute by G. D. Krasnozhen.

o-Nitroethylbenzene (V). A suspension of 200 g of the sulfate of (II) (m. p. 158-159°) in 600 ml of 15% sulfuric acid was treated as in the preparation of (IV). We obtained 12.6 g (16.2%) of o-nitroethylbenzene. After 5 vacuum distillations, we isolated 8.1 g of pure o-nitroethylbenzene. The clear, light yellow liquid had b. p. 76-77° (2 mm), 228-229° (752 mm), solidification temperature −11°, n_D^{20} 1.5356, d_4^{20} 1.1224. In contrast to the para-isomer, it rapidly acquired a red-brown color on storage.

m-Nitroethylbenzene (VI). A suspension of 126 g of the base (III) in 500 ml of 22% sulfuric acid was treated as in the preparation of (IV). We obtained 43.5 g (27.7%) of m-nitroethylbenzene. After 5 vacuum distillations, we isolated 33.5 g of pure m-nitroethylbenzene. The light yellow liquid had b. p. 91-92° (2.5 mm), 242-243° (752 mm), solidification temperature -37.9°, n_D^{20} 1.5390, d_4^{20} 1.1214. Like (V), it acquired a red-brown color on storage.

SUMMARY

1. We synthesized p-, o- and m-aminoethylbenzenes and defined the melting points of their salts (hydrochlorides, sulfates, and picrates).

2. We synthesized p-, o- and m-nitroethylbenzenes and defined their physicochemical constants (boiling and solidification points, specific gravities and refractive indices).

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CATALYTIC AMINATION OF ORGANIC COMPOUNDS

VI. AMINATION OF ESTERS OF ALIPHATIC ACIDS

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The reaction of esters and ammonia has not been studied sufficiently, although it has been examined in recent literature as a general method for preparing acid amides [1-5]. It was established that the amination of esters proceeded much more readily when compressed ammonia was used for this purpose. Recently, especially in patent literature, there have also been indications that passing ester vapor in a current of ammonia over a heated dehydrating catalyst (aluminum and thorium oxides etc.) gives acid nitriles and, in a series of cases, unsaturated hydrocarbons in addition [6-11].

In this work we decided to investigate the latter reaction more thoroughly in order to obtain nitriles and amines from esters and ammonia, as the former substances have found practical application in the synthesis of artificial fibers, plasticizers etc. The esters were aminated by passing ester vapors in a current of ammonia at various pressures, over a heated catalyst in the apparatus used by us in the previous work [12].

We investigated seven different esters (see Table). As catalysts we tried active granulated aluminum oxide, aluminum oxide with 10% silicon oxide and factory-manufactured glassy silica. Aluminum oxide was found to be most active; additions of thorium or silicon oxides did not increase the catalyst activity. The silicon oxide was found to be a weak catalyst.

In all the cases we studied in the reaction of ammonia with esters we observed the formation of the corresponding amine from the alcoholic radical and nitrile from the acid radical.

$$R—COOR' + 2NH_3 \rightleftharpoons R—CN + R'NH_2 + 2H_2O$$

Actually, the reaction proceeded through the formation of a series of intermediate products. The amines formed by this reaction were a mixture of primary, secondary and tertiary amines.

EXPERIMENTAL

Experiments on the amination of esters were carried out by the following method. A 30-40 g sample of the material was passed at a rate of 10-20 drops a minute in a stream of ammonia over the catalyst, heated to 250-400°. The ammonia pressure was kept in the range 1-10 atm due to the pressure in the tank. The gaseous reaction products were trapped separately from the liquid catalyzate. With cooling, the catalyzate was carefully acidified with HCl (1:3) to a weakly acid reaction and then steam distillation of it yielded a neutral fraction, from which the nitrile was isolated by distillation. The residue from the isolation of the neutral fraction was made strongly alkaline and the amines steam distilled, salted out from the distillate, dried, distilled and analyzed by the method of K. G. Mizuch and A. Ya. Savchenko [13]. The secondary and tertiary amines were calculated as primary amine.

One of the most characteristic experiments is described as an example. 38 g of butyl acetate (b. p. 124-125°, n_D^{20} 1.3976, d_4^{20} 0.8816) was passed at a rate of 10 drops a minute in a stream of ammonia over aluminum oxide, heated to 370-380°. The ammonia pressure was 9 atm during the experiment. 43 ml of catalyzate was collected in the receiver and 3 liters of gas was obtained in the gas collector. The catalyzate yielded 17.5 g

of amines, which distilled in the range 75-170°. On analyzing the amines, we found 58.2% of primary, 29.0% of secondary and 12.8% of tertiary amine. Distillation of the amines obtained from several experiments gave butylamine and dibutylamine in a pure form. Tributylamine could not be obtained in a pure form by distillation. The neutral reaction products yielded 9.3 g of acetonitrile (b. p. 79-81°, d_4^{20} 0.783, n_D^{20} 1.343) and 7.0 g of unreacted butyl acetate. The yield of nitrile was 69.4% on the ester taken and 85.3% on that which reacted. The yield of amine was 77.1% on the ester taken and 94.7% on that which reacted.

Expt. No.	Name of ester	Experiment temperature	Yield of nitrile (%)		Yield of amines (%)		Amount of gas (in liters)
			on ester taken	on reacted ester	on ester taken	on reacted ester	
1	Butyl acetate	250°	11.1	36.4	13.2	43.4	0.5
2		300	31.7	63.4	39.0	77.5	2.5
3		370	47.3	82.9	46.7	81.9	5.0
4		370	69.1	85.3	77.1	94.5	4.5
5		370	11.1	14.7	12.7	17.1	10.0
6		410	16.4	24.2	21.2	31.5	8.0
7	Isobutyl acetate	370	38.7	52.2	39.5	53.6	4.5
8		370	63.1	89.6	68.5	97.5	2.0
9	Isoamyl acetate	370	10.8	15.3	8.5	11.9	10.0
10		370	24.4	39.6	24.3	39.5	7.0
11		370	49.7	61.1	48.4	59.6	5.5
12		370	69.1	74.6	72.2	78.3	4.5
13	Propyl propionate	370	60.4	81.8	67.3	91.7	3.0
14	Butyl propionate	370	61.9	73.8	74.4	90.9	3.0
15	Propyl butyrate	370	32.9	55.2	43.5	73.3	3.0
16	Butyl butyrate	370	53.8	70.3	67.5	87.5	3.0

*All the experiments were carried out at an ammonia pressure of 9 atm, except for experiments 5 and 9, which were carried out at 1 atm and experiment 10 at 4 atm. All the experiments were performed with a rate of 20 drops a minute except experiments 4 and 9, where the rate was 10 drops a minute. In all the experiments an aluminum oxide catalyst was used.

The yield of amines and nitriles depended on the ammonia pressure, the temperature, the chemical composition of the catalyst and the chemical structure of the ester. The results of our experiments are given in the Table. The following conclusions may be drawn from the data in the Table. The ammonia pressure in the reaction zone has an exceptionally great effect on the yield of the reaction end products; at an ammonia pressure of one atmosphere, the yield of amines and nitriles is very small; a large amount of gas of an unsaturated nature is formed in this case, indicating that there is considerable decomposition of the ester or the reaction products. At an ammonia pressure of 9 atm the yield of amines and nitriles considerably increased and the amount of gaseous reaction products decreased.

The yield of amines and nitriles reached a maximum at a temperature of 370-380°. With a further increase in temperature, the yield of amines and nitriles fell considerably and at the same time the amount of gaseous reaction products increased.

The chemical structure of the ester also had an effect on the yield of amines and nitriles, but it is not possible to formulate this as a definite law at the moment.

SUMMARY

We studied a method of amine and nitrile synthesis using the catalytic amination of esters with compressed ammonia in a flow system. We established the reaction of reaction product yields to the temperature of the experiment and the ammonia pressure in the reaction zone.

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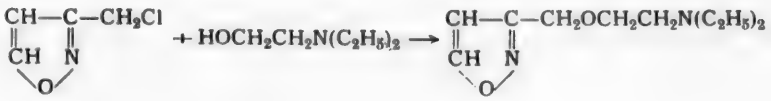
INVESTIGATION IN THE ISOXAZOLE SERIES

IV. SYNTHESIS OF SOME AMINES OF THE ISOXAZOLE SERIES

N. K. Kochetkov, E. D. Khomutova, M. Ya. Karpeisky and R. M. Khomutov

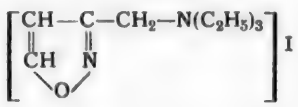
Recently one of us and A. F. Khorlin [1] described the preparation of 3-chloromethylisoxazole and its properties and reactions, characterizing the lability of the halogen atom. Among other reactions, it was shown that the chlorine atom in 3-chloromethylisoxazole was readily exchanged for a dialkylamino group. As physiologically active substances containing the isoxazole ring have been obtained recently [2], we decided to synthesize some derivatives of the isoxazole series, containing an amino group in the side chain. Thus, 3-chloromethylisoxazole reacted with diethylaminoethanol to give (isoxazolyl-3-methyl)-β-diethylaminoethyl ether.



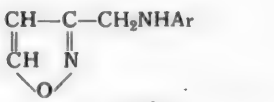
The amino ether obtained reacted with ethyl iodide in the cold to form a quaternary salt, which also confirmed its structure.

Under the same conditions 3-diethylaminomethylisoxazole readily gave a quaternary salt (I) with ethyl iodide, while direct reaction of 3-chloromethylisoxazole with triethylamine did not give the desired result.

We then succeeded in condensing 3-chloromethylisoxazole with aromatic amines in order to use the compounds obtained (II) for synthesizing isologs of the known antihystamine preparation "antergan," which contain an isoxazole ring instead of a benzene nucleus.



(I)

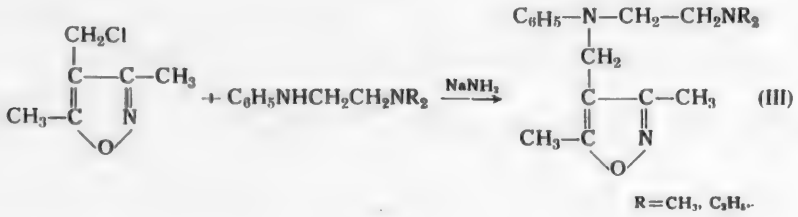


(II) Ar = C_6H_5, o-$CH_3C_6H_4$

The reaction proceeded smoothly on heating 3-chloromethylisoxazole with excess aniline in the presence of an aqueous solution of sodium bicarbonate. However, we could not isolate the required substance by reacting phenylaminomethylisoxazole with dialkylaminoethyl chloride in the presence of sodamide. This result may be explained by our using a monosubstituted isoxazole, which, as is known, cannot stand heating with strong alkaline reagents [3]. Condensation of 3-chloromethylisoxazole with N-phenyl-N',N'-dialkylethylenediamine was also unsuccessful for the same reason. We therefore decided to synthesize dialkylchloromethylisoxazole as, according to the literature data, trisubstituted isoxazoles are stable to the action of alkaline reagents [4]. However, up to now substituted halomethylisoxazoles have been extremely inaccessible and they may be prepared only by a multistage method, of no preparative value [5]. We succeeded in developing a simple and convenient method for preparing 4-chloromethyl-3,5-dimethylisoxazole, consisting of the chloro-

methylation of the readily available 3,5-dimethylisoxazole [6]. This reaction, which is new for N-containing heterocyclic compounds, among them isoxazole, was carried out by heating 3,5-dimethylisoxazole with paraformaldehyde in dry carbon tetrachloride in the presence of hydrogen chloride. The 3,5-dimethyl-4-chloromethylisoxazole yield was 28-30%. The chloromethylation of isoxazole has quite a general character.

3,5-Dimethyl-4-chloromethylisoxazole was condensed with N-phenyl-N',N'-dialkylethylenediamine by heating the Na-derivatives of the amines with 3,5-dimethyl-4-chloromethylisoxazole in a xylene medium.



The physiological activity of the compounds obtained was tested in the Pharmacological Section of the Institute of Pharmacology and Chemotherapy of the Academy of Medicine. Compound (I) had a slight cholinolytic activity rather than the cholinomimetic activity expected in comparison with furamone. Compound (III) had a weak antihystamine activity.

EXPERIMENTAL

Isoxazolyl-3-methyl-β-diethylaminoethyl ether. 50 ml of absolute diethylaminoethanol, in which 2.3 g of sodium had been dissolved, was placed in a three-necked flask fitted with a mechanical stirrer, a dropping funnel and a reflux condenser with a calcium chloride tube. While the reaction mixture was cooled in a mixture of ice and salt, 11.7 g (0.1 mole) of 3-chloromethylisoxazole [1] in 25 ml of diethylaminoethanol was added dropwise. The thickened reaction mixture was stirred for 4 hours at room temperature, 100 ml of absolute ether added and the sodium chloride filtered off. The ether was distilled off from the filtrate and the residual oil vacuum distilled to give a fraction 110-112° (8 mm). After a second distillation, the ether obtained had b. p. 83-84° (1 mm), n_D^{20} 1.4623, d_4^{20} 1.0146. A test for halogen was negative.

Found %: N 14.19, 13.92; C 61.65, 61.72; H 9.18. $C_{10}H_{18}O_2N_2$. Calculated %: N 14.06; C 61.85; H 9.27.

Isoxazolyl-3-methyl-β-diethylaminoethyl ether was a colorless, mobile oil, which darkened in air.

Isoxazolyl-3-methyl-β-diethylaminoethyl ether ethiodide. A mixture of 2 g of the aminoether and 1.6 g of ethyl iodide was shaken in the dark at room temperature for 2-3 days, diluted with ether and filtered. After recrystallization from a mixture of alcohol and ether, the ethiodide obtained had m. p. 82-83°; the yield was quantitative.

Found %: N 7.79, 7.71; C 40.40, 40.37; H 6.50, 6.47. $C_{12}H_{23}O_2N_2I$. Calculated %: N 7.90; C 40.68; H 6.54.

The colorless, crystalline substance was readily soluble in water and alcohol. It decomposed in light.

3-Diethylaminomethylisoxazole ethiodide. This was prepared as described above from 3.0 g of 3-diethylaminomethylisoxazole and 4.0 g of ethyl iodide. Recrystallization from a mixture of alcohol and ether yielded a colorless, crystalline substance with m. p. 131-132° in 60-65% yield.

Found %: N 9.58, 9.59; C 38.99, 39.02; H 6.20, 6.23. $C_{10}H_{19}ON_2I$. Calculated %: N 9.03; C 38.72; H 6.17.

Isoxazolyl-3-methylaniline. 0.4 mole of aniline, 10.5 g (0.125 mole) of sodium bicarbonate and 10 ml of water were placed in a three-necked flask, fitted with a mechanical stirrer, a dropping funnel and a reflux condenser. The mixture was heated on a boiling water bath and stirred vigorously while 11.7 g (0.1 mole) of chloromethylisoxazole was added dropwise. The reaction mixture was heated and stirred for a further 4 hours, cooled and filtered and the aqueous layer separated; the mixture of amines was washed with a saturated solution of sodium chloride, shaken with magnesium sulfate and vacuum distilled to give a fraction with b. p. 152-154° (2 mm), which completely crystallized in the receiver. After recrystallization from petroleum ether, the isoxazolyl-3-methylaniline had m. p. 63-64°; the yield was 80-85%.

Found %: N 16.39, 16.51; C 69.20, 69.18; H 5.80, 5.87. $C_{10}H_{10}ON_2$. Calculated %: N 16.08; C 68.94; H 5.78.

The white, crystalline substance, which darkened in air, was readily soluble in alcohol and benzene and insoluble in water.

Isoxazolyl-3-methyl-o-toluidine was prepared similarly from 40.3 g (0.4 mole) of freshly distilled o-toluidine and 11.7 g (0.1 mole) of chloromethylisoxazole in the presence of a solution of 10.5 g of sodium bicarbonate in 10 ml of water. Distillation in vacuum yielded a fraction with b. p. 145-150° (1 mm) which completely crystallized on standing; the m. p. was 80-81°.

Found %: N 15.10, 15.17; C 70.30, 70.36; H 6.48, 6.50. $C_{11}H_{12}ON_2$. Calculated %: N 14.89; C 70.18; H 6.42.

3,5-Dimethyl-4-chloromethylisoxazole. 50 ml of dry carbon tetrachloride, 7.5 g of paraformaldehyde, 10.0 g of anhydrous zinc chloride and 22.4 g of 3,5-dimethylisoxazole were placed in a three-necked flask, fitted with a mechanical stirrer, a gas inlet and a reflux condenser. A stream of dry hydrogen chloride was passed through the reaction mixture at 50-60° for 1.5 hours, after which the reaction mixture was stirred at the same temperature for a further 3 hours, cooled, poured into 300 ml of water and the carbon tetrachloride layer separated; the aqueous layer was neutralized with sodium carbonate solution and extracted three times with ether. The ether extracts were combined with the carbon tetrachloride layer and washed with water, sodium bicarbonate solution and again with water. The solvent was distilled off on a fractionating column and the residual oil vacuum distilled to give a fraction with b. p. 103-105° (20 mm). After a second distillation, the substance had b. p. 87-88° (8 mm), n_D^{20} 1.4858, d_4^{20} 1.1730; the yield was 28-30%.

Found %: Cl 24.58, 24.50; C 49.70, 49.65; H 5.60, 5.58. C_6H_8ONCl. Calculated %: Cl 24.39; C 49.49; H 5.53.

3,5-Dimethyl-4-chloromethylisoxazole was a colorless, mobile oil, which became yellow on standing, was strongly lachrimatory and formed a complex with urotropine.

N-Phenyl-N-(3,5-dimethylisoxazolyl-4-methyl)-N',N'-dimethylethylenediamine. 75 ml of dry xylene, 2.5 g of powdered sodamide and 8 g of N-phenyl-N',N'-dimethylethylenediamine [7], were placed in a three-necked flask, fitted with a mechanical stirrer, a dropping funnel and a reflux condenser, the mixture boiled until the evolution of ammonia ceased and cooled and 7 g of 3,5-dimethyl-4-chloromethylisoxazole in 20 ml of dry xylene added dropwise with stirring. The reaction mixture was heated for 4 hours at 80-90°, cooled, mixed with 100 ml of 10% sodium hydroxide solution, the xylene layer separated and the aqueous layer extracted with benzene. The combined extracts were dried over potassium carbonate, the solvent distilled off in vacuum and the residual oil distilled to give a fraction with b. p. 172-175° (1-1.5 mm); the yield was 40%. The substance was a very viscous orange oil, which quickly darkened in air. The N-phenyl-N-(3,5-dimethylisoxazolyl-4-methyl)-N',N'-dimethylethylenediamine obtained was dissolved in anhydrous ether and a stream of dry hydrogen chloride passed through with cooling. The dihydrochloride was obtained as colorless, slightly hygroscopic crystals. After recrystallization from a mixture of alcohol and ether, the substance had m. p. 141-142°.

Found %: N 11.90, 12.15; Cl 20.40, 20.39; C 55.38, 55.40; H 7.25, 7.23. $C_{16}H_{25}ON_3Cl_2$. Calculated %: N 12.15; Cl 20.47; C 55.48; H 7.27.

N-Phenyl-N-(3,5-dimethylisoxazolyl-4-methyl)-N',N'-diethylethylenediamine. This was prepared similarly from 13.2 g of N-phenyl-N',N'-diethylethylenediamine, 2.2 g of sodamide and 10 g of 3,5-dimethylisoxazole in 75 ml of xylene. Vacuum distillation yielded a fraction with b. p. 162-170° (1 mm); the yield was 35%. After recrystallization from alcohol, the dihydrochloride had m. p. 127-128°.

Found %: N 11.30, 11.40; Cl 18.81, 18.90. $C_{18}H_{29}ON_3Cl_2$ Calculated %: N 11.38; Cl 18.94.

The dihydrochloride formed white, hygroscopic crystals.

SUMMARY

1. It was established that 3,5-dimethylisoxazole may be chloromethylated to give 3,5-dimethyl-4-chloromethylisoxazole.

2. It was shown that N-phenyl-N-(3,5-dimethylisoxazolyl-4-methyl)-N',N'-dialkylethylenediamines and 3-diethylaminomethylisoxazole ethiodide obtained by us have a slight physiological activity.

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INVESTIGATIONS IN THE FIELD OF THIOINDIGOID DYES

I. SYNTHESIS OF THIOPHENOLS AND S-ARYLTHIOGLYCOLIC ACIDS

G. M. Oksengendler* and Yu. E. Gerasimenko

A paper in the literature [1] describes a method for preparing thiophenols by reacting diazonium salts with sodium or potassium polysulfides followed by the reduction of the diaryl polysulfides obtained with metals in an acid medium. Using this method as a basis, we developed a convenient method for preparing thiophenols and the S-arylthioglycolic acids corresponding to them. We found that aryldiazonium chlorides reacted with sodium polysulfide to give, in addition to diaryl polysulfides, 5-10% of diarylsulfides as side products. It is interesting to note that these diazo compounds reacted with sodium disulfide to give mainly diaryl sulfides. The yield of them was about 60% and that of diaryl disulfides was only about 30%. The reduction of diaryl polysulfides with metals in an acid medium was inconvenient as this process took a long time and was accompanied by the evolution of hydrogen sulfide. In this work we investigated the conversion of diaryl polysulfides to thiophenols by treatment with aqueous alkali. This method has not been described in the literature. As a result of the experiments it was found that when using diaryl polysulfide molecules without substituents, which made them soluble in alkali, the conversion temperature must be 120-150°, which was achieved either by using a concentrated (40%) aqueous solution of sodium hydroxide or by carrying out the process under pressure.

The reduction scheme may be represented as follows. First of all, the labile sulfur atoms in the diaryl polysulfide molecule are split off by the action of sodium hydroxide and form sodium sulfide. Then the sodium sulfide in an alkaline medium acts as a reducing agent. The overall reaction for diaryl tetrasulfide may be expressed by the following equation:

$$4Ar_2S_4 + 18NaOH = 8ArSNa + 2Na_2S + 3Na_2S_2O_3 + 9H_2O.$$

If necessary, the thiophenols may be isolated from the alkaline solution by careful acidification. However, in most cases they were not isolated and were condensed with monochloroacetic acid to give the corresponding S-arylthioglycolic acids by the scheme

$$ArSNa \xrightarrow{ClCH_2COONa} ArSCH_2COONa \xrightarrow{HCl} ArSCH_2COOH$$

The yields of thiophenols and S-arylthioglycolic acids, corresponding to them, reached 80% of the theoretical.

Twelve S-arylthioglycolic acids were synthesized by the given method; of these the following have not been described in the literature: S-(p-hydroxyphenyl)-thioglycolic acid, S-(p-methoxyphenyl)-thioglycolic acid, S-(p-ethoxyphenyl)-thioglycolic acid, S-(2,4-dimethylphenyl)-thioglycolic acid, S-(2-methyl-4-iodophenyl)-thioglycolic acid and S-(2,4-dibromophenyl)-thioglycolic acid.

*Deceased.

Initial amine	Name of aryl in the S-arylthioglycolic acid ArSCH$_2$COOH	Yield (in %)	Melting point		Formula	Analysis		
			our data	literature data		element	found %	calculated %
Aniline	Phenyl	60	62° •	62° [1]	$C_8H_8O_2S$		—	—
o-Toluidine	o-Tolyl	68.2	108—109 •	108—109 [3]	$C_9H_{10}O_2S$		—	—
m-Toluidine	m-Tolyl	83	104 •	104 [5]	$C_9H_{10}O_2S$		—	—
p-Toluidine	p-Tolyl	65.7	95 •	95 [3]	$C_9H_{10}O_2S$		—	—
2,4-Dimethylaniline	2,4-Dimethylphenyl	41.5	123.7 •	—	$C_{10}H_{12}O_2S$	C	61.4, 61.3	61.16
						S	16.4, 16.5	16.33
p-Aminophenol	p-Hydroxyphenyl	—	144.7—145 ••	—	$C_8H_8O_3S$	C	52.4, 52.3	52.14
						S	17.3, 17.2	17.40
p-Anisidine	p-Methoxyphenyl	75.3	75 ••	—	$C_9H_{10}O_3S$	S	16.8, 16.3	16.15
p-Phenetidine	p-Ethoxyphenyl	71.8	64—64.5 ••	—	$C_{10}H_{12}O_3S$	C	56.5, 56.6	56.57
						S	15.0 —	15.10
p-Phenoxyaniline	p-Phenoxyphenyl	82.7	74—75 ••	73—74 [6]	$C_{14}H_{12}O_3S$			—
2-Methyl-4-iodaniline	2-Methyl-4-iodophenyl	62	115—116 ••	—	$C_9H_9O_2IS$	S	10.3, 10.4	10.40
2,4-Dibromoaniline	2,4-Dibromophenyl	46	139.5—140 ••	—	$C_8H_6O_2Br_2S$	S	9.7, 9.6	9.83
						Br	47.4, 47.6	49.01
α-Naphthylamine•••	α-Naphthyl	40—45	107 •	111—112 [7]	$C_{12}H_{10}O_2S$		—	—

• After recrystallization from water.

•• After recrystallization from toluene.

••• Dinaphthyl polysulfide formed very vigorously, though no explosions were observed in any of the cases.

EXPERIMENTAL

0.1 mole of o-toluidine hydrochloride was dissolved in 50 ml of water and 20 g of 27.5% hydrochloric acid, cooled to 0° and 7.25 g of sodium nitrite in 15 ml of water was slowly added. The diazo solution was cooled to −5° and slowly added over a period of 1/2 an hour to a solution of sodium tetrasulfide, heated to 60° and vigorously stirred. The latter was prepared in the following way: 10.4 g of sulfur was added to 9.75 g of sodium sulfide in 40 ml of water, the mixture boiled until solution was complete, then filtered and 6 g of calcined sodium carbonate added. During the addition of the diazo solution to the sodium tetrasulfide solution, there was vigorous, characteristic decrepitation — an indication of diazopolysulfide decomposition. Due to the danger of explosion, it is necessary to avoid an accumulation of the latter in the reaction mixture (slow addition of the diazo solution, temperature not below 50°). A yellow-orange color in the mixture indicates the accumulation of diazopolysulfide. In this event it is necessary to stop the addition of diazo solution and wait until the color changes to brown. At the end of the reaction, the reaction mixture was cooled and the lower oily layer separated. The oily liquid was mainly di-(o-tolyl)-tetrasulfide and it was refluxed for 2 hours with 47 g of a 40% aqueous solution of sodium hydroxide. The boiling point had to be 120-122° and if it was lower, part of the water was distilled off. The reduction could be carried out in an autoclave at 150° for 1 hour. The reaction mixture was diluted with 200 ml of water, acidified to pH 8-9 and extracted with ether; the ether extract was dried, the ether distilled off and the o-thiocresol vacuum distilled. The yield was 6.8 g (55%, calculated on the o-toluidine hydrochloride).

S-(o-Tolyl)-thioglycolic acid was prepared without isolating the o-thiocresol from the reaction mixture. The mixture was diluted with 100 ml of water and 25 g of monochloroacetic acid added at 20-30°. When it no longer gave a brown stain with lead acetate paper, the alkaline solution was filtered. There remained on the filter 1-2 g of material, which was recrystallized from alcohol and identified as di-(o-tolyl)-sulfide (m. p. 64°, agreeing with literature data [2]). Acidification of the filtrate yielded S-(o-tolyl)-thioglycolic acid.

By reprecipitation from sodium carbonate solution, we obtained 12.4 g of S-(o-tolyl)-thioglycolic acid with m. p. 107-108°.

Under similar conditions, but substituting the sodium tetrasulfide solution by a sodium disulfide solution (9.75 g of sodium sulfide, 40 ml water and 4 g of sulfur was boiled to give a solution, which was filtered and 6 g of calcined sodium carbonate added), we obtained about 13 g (60%) of di-(o-tolyl) sulfide with b. p. 63-64° (from alcohol) and 5.5 g (30%) of S-(o-tolyl)-thioglycolic acid, which corresponds to the formation of not less than 30% of di-(o-tolyl) disulfide.

The results of synthesizing S-arylthioglycolic acids by the method described are given in the Table.

S-(p-Hydroxyphenyl)-thioglycolic acid was synthesized by a modified method. 0.1 mole of p-aminophenol was diazotized and the diazo solution added to a solution of 7.4 g of sodium disulfide and 5.6 g of sodium hydroxide in 40 ml of water at 20°. The mixture was heated to 85-90°, kept there for 1/2 hour, cooled to 20° and diluted with 100 ml of water and 0.5 g of sodium hydrosulfite, 4 g of sodium hydroxide and 15 g of monochloroacetic acid added. After 2 hours, the reaction mixture was acidified to pH 8 and the p,p'-dihydroxydiphenyl sulfide with m. p. 151° (from water) filtered off. The filtrate was acidified and the precipitate filtered off, washed with a small amount of water and dried. The slightly yellowish crystals were readily soluble in cold water, very readily soluble in alcohol and hot water and difficultly soluble in hot toluene. The structure of the acid was proved by synthesis. 0.05 mole of S-(p-nitrophenyl)-thioglycolic acid was reduced with zinc dust in 12% sulfuric acid. The zinc carbonate was precipitated with sodium carbonate and filtered off, the solution of S-(p-aminophenyl)-thioglycolic acid acidified with sulfuric acid and diazotized at 0°, the excess nitrous acid removed with urea and the solution slowly poured into a 30% solution of sulfuric acid, heated to 60°. After the disappearance of the diazo compound (after 12 hours), the reaction mixture was cooled and the precipitate filtered off. The m. p. was 145° (from water). A mixed melting point with the substance obtained from the p-aminophenol was not depressed.

SUMMARY

1. A convenient method was found for preparing thiophenols by heating diaryl polysulfides with an aqueous solution of sodium hydroxide.

2. The thiophenols obtained were converted to S-arylthioglycolic acids. We synthesized 12 S-arylthioglycolic acids and, of them, 6 are described for the first time.

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THE REACTION OF 3-PHENYLOXAZOLIDINE WITH PHENOL, 2,6-DIMETHYLPHENOL AND 2,4-DIMETHYLPHENOL

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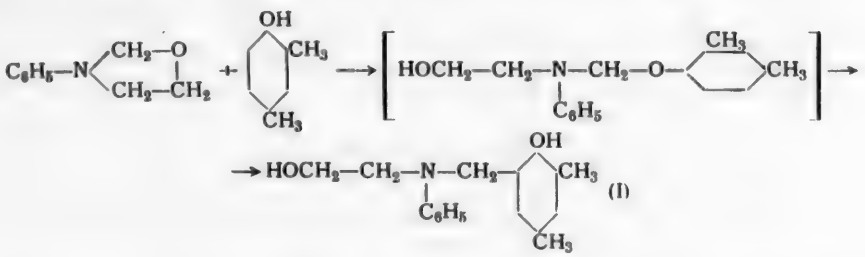
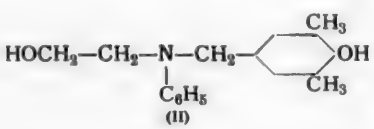
No information is given in literature on the reaction of oxazolidine with phenols (see monograph [1]). We observed this reaction for the first time in 1950 [2]. It was studied in greater detail from the examples of the reaction of 3-phenyloxazolidine with 2,4-dimethylphenol, 2,6-dimethylphenol and phenol.

By heating 3-phenyloxazolidine with 2,4-dimethyldiphenol we obtained 2,4-dimethyl-6-(β-hydroxyethylphenylaminomethyl)-phenol (I) in the form of a thick brownish oil; it was probably formed according to the following system (comp. [3, 4]:



The product obtained was soluble in alkalis. This indicates the presence of a free phenolic hydroxyl group in it and serves to confirm its structure. In addition, the structure of the substance was confirmed by the analysis of its carbon, hydrogen and nitrogen contents and by the determination of its hydroxyl groups by Tserevitinov's method.

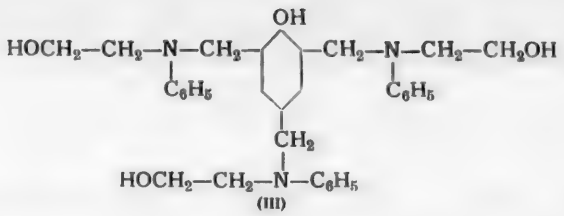
2,6-Dimethyl-4-(β-hydroxyethylphenylaminomethyl)-phenol (II) was obtained by the reaction of 3-phenyl-



(II)

oxazolidine with 2,6-dimethylphenol; this compound was also soluble in alkalis.

As regards the reaction of phenol with 3-phenyloxazolidine, the formation of 3 compounds – with one, two and three molecules of 3-phenyloxazolidine – is possible in this instance. We investigated the compound of phenol with three molecules of 3-phenyloxazolidine, with the empirical molecular formula $C_{33}H_{39}O_4N_3$, in greater detail. This compound was obtained by heating phenol with 3-phenyloxazolidine in a ratio of 1:3 and 1:3.2. It was completely soluble in alkalis which indicates the presence of a free phenolic hydroxyl group. The value found for its molecular weight (by Rast's method) agreed with the theoretical value. On this basis the compound with the composition $C_{33}H_{39}O_4N_3$ may be given the structure of 2,4,6-tri-(β-hydroxyethylphenylaminomethyl)-phenol (III).



(III)

The formation of compound (III) from phenol and 3-phenyloxazolidine conceivably takes place as follows: phenol, evidently, is first added coordinately to 3-phenyloxazolidine. When this takes place the oxazolidine ring is ruptured and an intermediate product $C_6H_5-O-CH_2-N(C_6H_5)-CH_2-CH_2OH$ is formed; this then undergoes rearrangement to β-hydroxyethylphenylaminomethylphenol.

$$HOC_6H_4-CH_2-N(C_6H_5)-CH_2CH_2OH.$$

The β-hydroxyethylphenylaminomethylphenol, reacting with 3-phenyloxazolidine in the above-mentioned sequence, is then converted to di-(β-hydroxyethylphenylaminomethyl)-phenol and the latter then condenses with 3-phenyloxazolidine, forming (III)

In this connection it must be mentioned that ethers of phenols (for example, anisole) in which the hydrogen of the phenolic hydroxyl is replaced by alkyl do not react with 3-phenyloxazolidine. This, to some extent, is evidence in favor of the above-mentioned opinion regarding the mechanism of the formation of β-hydroxyethylphenylaminomethylphenols from phenols and 3-phenyloxazolidine.

We also investigated the reaction of oxazolidines with novolaks (mesomethylenepolyphenols). In this case the reaction takes place with the formation of resinoid products of industrial value [2] (comp. [5]).

EXPERIMENTAL

2,4-Dimethyl-6-(β-hydroxyethylphenylaminomethyl)-phenol (I). 149 g (1 mole) of 3-phenyloxazolidine and 132 g (1.08 mole) of 2,4-dimethylphenol were placed in a three-necked flask, equipped with a stirrer and reflux condenser, and the mixture was heated on a glycerin bath at 110-120° for 36 hours. When the process was completed the highly-volatile matter was steam distilled until a negative reaction for 2,4-dimethylphenol was given with Millon's reagent. After this the product was distilled under vacuum, the 2,4-dimethyl-6-(β-hydroxyethylphenylaminomethyl)-phenol being collected within the temperature range of 225-230° at 2 mm. 73 g of a light-brown viscous oil, soluble in ethyl alcohol, hydrocarbons and alkalis, was obtained.

Found %: C 75.30, 75.40; H 7.46, 7.37; N 5.12; OH 12.95, 13.16 (by Tserevitinov's method, in o-xylene). $C_{17}H_{21}O_2N$. Calculated %: C 75.27; H 7.74; N 5.17; OH 12.55.

2,6-Dimethyl-4-(β-hydroxyethylphenylaminomethyl)-phenol (II) was obtained by heating 17.1 g (0.115 mole) of freshly-distilled 3-phenyloxazolidine with 14 g (0.114 mole) of 2,6-dimethylphenol at 105-140° for 18 hours. The product was separated from the reaction mixture by fractionation and was collected within the limits of 240-260° at 2-3 mm. In external appearance the product obtained was a dark-brown oil. It crystallized after a certain time. After recrystallizing 3 times from benzene 2,6-dimethyl-4-(β-hydroxyethylphenylaminomethyl)-phenol had the appearance of white plates with an m. p. of 110.5-112°. 4.5 g of recrystallized product was obtained.

Found %: N 5.79. $C_{17}H_{21}O_2N$. Calculated %: N 5.17.

2,4,6-Tri-(β-hydroxyethylphenylaminomethyl)-phenol (III) was obtained by heating 238.4 g (1.6 mole) of 3-phenyloxazolidine and 47 g (0.5 mole) of phenol at 110-120° for 12 hours. The initial unreacted substances and other highly-volatile admixtures were steam distilled from the product. The latter was freed from moisture

by heating on a glycerin bath under vacuum which toward the end of the reaction was reduced to 7 mm while the temperature of the bath was brought to 120°. After the removal of the moisture the product was a light-yellow, brittle, transparent rosinlike mass with a softening point (in a capillary tube) of 55°. With further heating it gradually commenced to melt, being converted to a liquid at 75°.

Found %: C 72.90, 72.70; H 7.48, 7.45; N 7.46, 7.54. M 542.4, 548 (by Rast's method). $C_{33}H_{39}O_4N_3$. Calculated %: C 73.19; H 7.20; N 7.76. M 541.

2,4,6-Tri-(β-hydroxyethylphenylaminomethyl)-phenol was obtained with a 91.40% yield of the theoretical. It was soluble in pyridine, cyclohexanol and alkalis.

SUMMARY

The reaction of 3-phenyloxazolidine with phenols, taking place with the rupture of the oxazolidine ring and the formation of β-hydroxyethylphenylaminomethylphenols is described.

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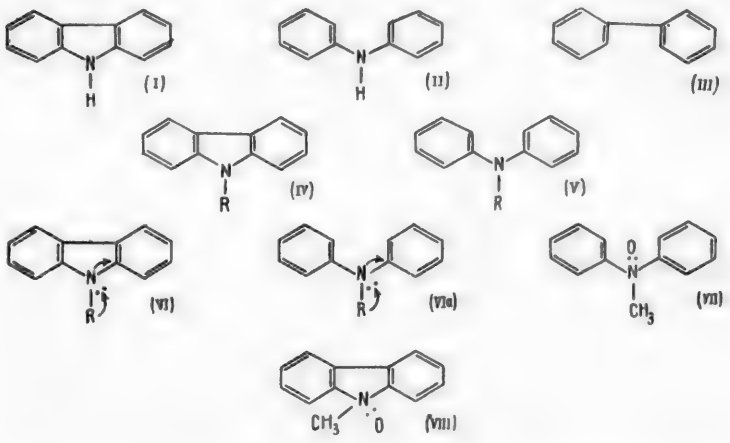
INVESTIGATION OF THE STRUCTURAL FEATURES AND CHEMICAL CONVERSIONS OF CARBAZOLE AND SOME OF ITS DERIVATIVES

I. ABSORPTION SPECTRA OF CARBAZOLE AND SOME OF ITS DERIVATIVES IN THE ULTRAVIOLET

S. I. Omelchenko, Z. V. Pushkareva and S. G. Bogomolov

Despite the potential possibilities of obtaining large amounts of carbazole (I) as a result of the scale of the coal-tar chemical industry at the present time, little use has been made until recently of coal-tar carbazole. One of the causes of the limited use of carbazole is the very peculiar nature of its chemical properties. The chemistry of carbazole, which, in the main, has already been worked out [1-3], still requires some clarification, principally as regards those reactions whose use would be of most practical advantage. Our research was directed at the investigation of the structural features, chemical conversions and methods for the practical utilization of some carbazole derivatives. As is known, the chemical properties of molecules are connected, in particular, with their electron state and the nature of conjugation; to explain the features of the carbazole molecule we, therefore, considered it useful to investigate the absorption spectra in the ultraviolet and, to a partial extent, in the visible regions. This paper gives the results of the investigation of the ultraviolet spectra of a specially selected group of substances.

Since the carbazole molecule simultaneously possesses the structure of diphenyl (III) and diphenylamine (II) the spectra of the latter were compared with the spectrum of carbazole; in addition, a mutual comparison was made between certain N-derivatives of carbazole (IV) and diphenylamine (V)



The spectra of the investigated substances were determined in an SF-4 quartz photoelectric spectrophotometer in a solution of anhydrous alcohol at concentrations of $10^{-3}-10^{-2}$ mole. The results of the measurements

are given in the form of curves, reflecting the variation of the extinction coefficient (ϵ) as a function of the wavelength, and also in Table 1.*

Name of compound	Thickness of the layer (in cm)	Maxima		Minima	
		λ (mμ)	log ε	λ (mμ)	log ε
Diphenyl	0.05	248	4.228	220	3.397
Diphenylamine	0.02	285	4.440	248	3.580
Carbazole	0.02	233	4.667	298	4.362
		241	4.434	250	4.254
		256	4.342	268	3.618
		292	4.288	304	3.447
		323	3.625	331	3.505
		336	3.574	—	—
N-Methyldiphenyl-amine	0.05	240	4.055	260	3.710
		290	4.130	—	—
N-Methylcarbazole	0.02	235	4.791	252	4.276
		260	4.505	274	3.860
		293	4.426	395	3.290
		329	3.748	338	2.638
		342	3.792	—	—
N-Carboxymethyl-carbazole	0.02	236	4.685	254	4.185
		258	4.295	270	3.715
		291	4.275	302	3.290
		322	3.600	330	3.560
		337	3.630	—	—
N-Acetyldiphenyl-amine	0.02	237	4.285	222	4.165
N-Acetylcarbazole	0.02	225	4.660	242	4.120
		258	4.312	295	3.810
		298	4.057	306	3.716
		310	3.903	—	—
N-Nitrosodiphenyl-amine	0.05	290	3.875	254	3.735
N-Nitrosocarba-zole	0.05	255	4.420	247	4.230
		280	4.170	265	4.035
		315	4.015	297	3.780
		330	4.060	400—720	2.640
N-Oxide of methyl-diphenylamine	0.1	256	3.105	250—252	3.060
		—	—	280—290	2.540
N-Oxide of methyl-carbazole	0.02	218	4.256	221—224	4.228
		233—235	4.252	252	2.041
		258	4.082	267—273	3.929
		291	4.060	315	3.322
		318—345	3.352	350—380	3.243
		390—395	3.342	—	—

The particular choice of the N-derivatives for investigation in this instance was made in order to determine the nature of the reaction of the electron system R with the aromatic rings (IV, V). A reaction of this type can only be represented as a $p\pi$-conjugation [4] with the participation of a noncovalent pair of electrons of the nitrogen atom as the conductor of the conjugation (VI or VIa). On this basis compounds, where R (in formulas IV or V) were either electron-donor or electron-acceptor substituents, were investigated. A comparison of the spectra of compounds (IV and V) with identical radicals made it possible to determine the influence of the second conductor of conjugation in the carbazole system, the $\pi\pi$-conjugation by a diphenyl bond, on the optical properties of the molecules.

N-Methyldiphenylamine (V, R = CH_3) [5] and N-methylcarbazole (IV, R = CH_3) were prepared as representatives of N-derivatives with electron-donor substituents. The substances with electron-acceptor properties included N-carboxymethyl-, N-acetyl- and N-nitroso derivatives. N-Carboxymethylcarbazole (IV, R = CH_2COOH)

* The spectra of some of the compounds we investigated had been previously investigated [12, 13], but for purely analytical purposes only. To carry out a comparative investigation of the series of compounds we had in mind, we had to use data obtained under identical conditions and in the same apparatus.

was obtained by reacting K-carbazole with ethyl chloroacetate [6]. N-Acetyldiphenylamine (V, R = $COCH_3$) and N-acetylcarbazole (IV, R = $COCH_3$) were obtained by acetylating (I) and (II) with acetic anhydride [7], the addition of sulfuric acid being employed in the latter instance [8]. The nitroso derivatives of diphenylamine [9] and carbazole [10] were made by the usual method.

To demonstrate experimentally the influence of the inclusion of p-electrons of the nitrogen atom in the conjugation system on the optical properties of the molecules, the N-oxide of methyldiphenylamine (VII) and the N-oxide of methylcarbazole (VIII) were prepared and investigated.

The N-oxide of methyldiphenylamine was obtained according to the method [11], namely by the oxidation of N-methyldiphenylamine with hydrogen peroxide in a solution of acetic anhydride. Oxides have not hitherto been obtained in the carbazole series. We tried to synthesize the N-oxide of methylcarbazole (VIII) by analogy with the above-mentioned method. Numerous attempts to synthesize the oxide by this method were, however, unsuccessful. The variation of the temperature conditions, the duration and other reaction conditions did not alter the result. We then tried to obtain the N-oxide of methylcarbazole by methods, specific for the preparation of N-oxides of heterocyclic compounds (by the oxidation of perbenzoic and perphthalic acids); here again, however, the result was usually the formation of tar. The N-oxide (VIII) was later obtained with a very poor yield by the oxidation of methylcarbazole with hydropyrite in glacial acetic acid.

On the basis of the data in Table 1 and from a comparative examination of the curves given in the diagrams the following conclusions and assumptions may be drawn. In Fig. 1, it is evident that with the transition from diphenyl to diphenylamine the importance is shown of the NH group as a typical auxochrome, intensifying the absorption intensity and displacing the absorption maximum into the long-wave region. With the transition from diphenylamine to carbazole (Fig. 1) the appearance of an additional conjugation line, simultaneously causing a planar structure of the molecule, leads to a substantial change in the absorption spectra in the ultraviolet region. The presence of the main maximum for carbazole (292 mμ) in the region of the only maximum for diphenylamine (285 mμ) is, however, characteristic.

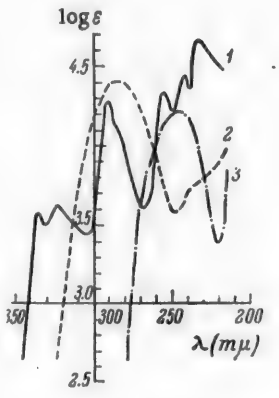


Fig. 1. Curves of the absorption spectra. 1) Carbazole; 2) diphenylamine; 3) diphenyl.

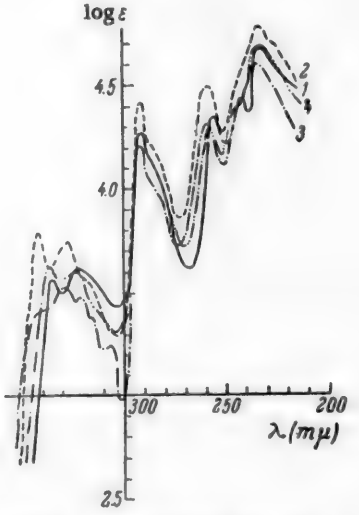


Fig. 2. Curves of the absorption spectra. 1) Carbazole; 2) N-methylcarbazole; 3) N-aminocarbazole; 4) N-carboxymethylcarbazole.

In the case of both carbazole and diphenylamine, substituents at the nitrogen atom exert a different influence on the spectrum, depending on their electron character. The introduction of groups such as methyl, carboxymethyl and amino groups does not lead to a change in the character of the spectral curve in the case of either carbazole (Fig. 2) or diphenylamine (Fig. 3); only the absorption intensity is somewhat changed.

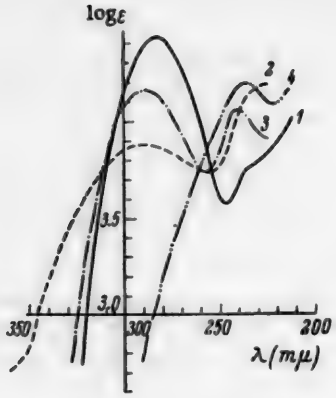


Fig. 3. Curves of the absorption spectra. 1) Diphenylamine; 2) N-nitrosodiphenylamine; 3) N-methyldiphenylamine; 4) N-nitrosodiphenylamine.

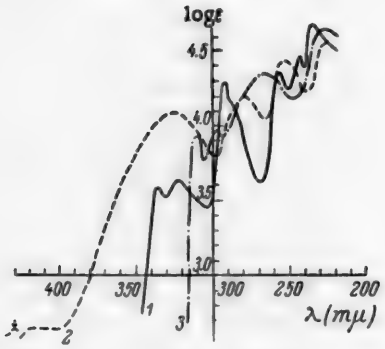


Fig. 4. Curves of the absorption spectra. 1) Carbazole; 2) N-nitrosocarbazole; 3) N-acetylcarbazole.

The introduction of electron-acceptor acetyl groups near the nitrogen (Figs. 3, 4) has a more powerful influence on the character of the spectra, which is shown by an abrupt displacement of the absorption toward the shortwaves. The carbazole spectrum (Fig. 4) undergoes a particularly marked change in this process; some of the secondary maxima disappear and the main maximum becomes broad and indistinct. A hypochromic effect also takes place.

A very interesting variation of the spectra is observed with N-nitroso derivatives of carbazole and diphenylamine (Figs. 4, 3). The introduction of a nitroso group leads to the appearance of a blurred, ill-defined spectrum, the curve apparently becomes broader in both directions and the absorption coefficients are decreased.

As was expected, the maximum variation of the optical properties was obtained from the oxidation of the heterocyclic nitrogen to N-oxides, when the noncovalent electron pair of atoms was occupied and the $p\pi$-conjugation was, as it were, discontinued. In the spectrum of the N-oxide of methyldiphenylamine (VII) (Fig. 5) the absorption band, characteristic of all the compounds we investigated containing an NH group, disappears. Only poorly-pronounced maxima are found in the 250-300 mμ region. The absorption intensity is considerably reduced and the absorption is displaced markedly into the short-wave region. In contrast to the previous instance the spectrum of the N-oxide of methylcarbazole (VIII) (Fig. 6) preserves the character of the spectrum of the initial N-methylcarbazole and the variation is only indicated by a marked reduction in the absorption intensity and in the bathochromic displacement of the absorption curve; the curve of N-methylcarbazole is, as it were, flattened. This difference in the absorption spectra of the two N-oxides may be explained by the fact that in the molecule of the N-oxide of methyldiphenylamine the aromatic rings are not actually conjugated, whereas in the molecule of the carbazole analog one of the conductors of conjugation remains (diphenyl bond).

EXPERIMENTAL

Carbazole. Technical carbazole with an m. p. of 232° was crystallized twice from ten times the quantity of xylene and once from 5 times the quantity of acetone. The product obtained with an m. p. of 238° was subjected to chromatography on aluminum oxide in a solution of benzene. The middle, weakly fluorescent layer was separated mechanically and elutriated with acetone. The acetone was distilled off and the residue obtained was recrystallized from benzene. The m. p. was 245°.

N-Methylcarbazole. Eight g of carbazole was suspended in 60 ml of acetone and 9.5 g of dimethylsulfate and 6 g of NaOH in 6 ml of water was added to the suspension with shaking. The mixture was shaken at room temperature for 1 hour. The solution formed was kept at 5-6° for 2 hours and was then diluted with 150 ml of water; the precipitate formed was filtered, washed with water and dried in air. The yield was 7 g (80.5%) the m. p. was 86°. For the spectroscopic investigations the product was recrystallized from alcohol; the m. p. was 89°.

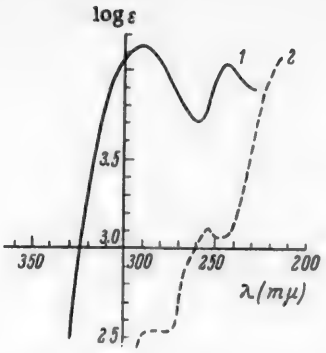


Fig. 5. Curves of the absorption spectra. 1) N-methyldiphenylamine; 2) N-oxide of N-methyldiphenylamine.

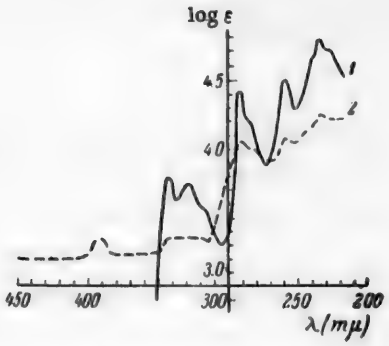


Fig. 6. Curves of the absorption spectra. 1) N-methylcarbazole; 2) N-oxide of N-methylcarbazole.

N-Carboxymethylcarbazole. a) K-Carbazole. A finely-ground mixture of 10 g of carbazole and 10 g of KOH was introduced into a copper crucible, first heated to 250° in Wood's alloy; the mixture melted rapidly. After being kept at 250° for 20 minutes the reaction mass was cooled; the upper layer of K-carbazole was easily separated. The yield was 11.9 g (96%). K-Carbazole was very hygroscopic and rapidly deliquesced in air.

b) 10 g of K-carbazole was mixed in the cold with 75 ml of ethyl chloroacetate and the mixture was boiled for 6 hours; the precipitate of N-carboxymethylcarbazole obtained was recrystallized from alcohol (m. p. 110°), then boiled with 200 ml of a 30% solution of NaOH, the alcohol was distilled off, 500 ml of water was added and the residue of unreacted carbazole was filtered. After acidification with 10% hydrochloric acid fine white crystals of N-carboxymethylcarbazole were precipitated from the filtrate. The yield was 4.5 g (35%), the m. p. was 214°. For spectroscopic measurements the acid obtained was purified by reprecipitation and then by crystallizing twice from chloroform and ethyl acetate. The m. p. was 216.5°.

N-Oxide of N-methylcarbazole. 5 g of N-methylcarbazole was dissolved with slight heating in 80 ml of glacial acetic acid and 15 g of 30% H_2O_2 in the form of finely ground tablets of hydropyrite was added to the solution with cooling and stirring. The mixture was kept at room temperature for 5 days and the solution was made alkaline with a 40% solution of KOH, while it was cooled intensely, until it gave a weakly-alkaline reaction; the precipitate which formed was filtered. The filtrate was transferred to a separating funnel and extracted with chloroform. The orange-colored chloroform extract was dried with calcined Na_2SO_4 and the chloroform was evaporated. The brown residue obtained was recrystallized from benzene. After standing for 12 hours a small amount of an orange-colored precipitate was deposited from the benzene solution and it was filtered and dried in a vacuum desiccator. 40 mg of the N-oxide of methylcarbazole with an m. p. of 187° was obtained. The melting point was not increased after a second crystallization from benzene.

Found %: N 6.87. $C_{13}H_{11}ON$. Calculated %: N 7.10.

SUMMARY

1. Ten derivatives of carbazole and diphenylamine were synthesized and the absorption spectra in the ultraviolet region for 13 compounds were investigated.

2. It was shown that with the transition from diphenylamine derivatives to carbazole derivatives the appearance of an additional conductor of conjugation (diphenyl bond), causing a planar structure of the molecule, leads to a substantial change of the absorption spectra in the ultraviolet.

3. Substituents at the nitrogen atom in both carbazole and diphenylamine exert a different influence on the absorption spectra, depending on their electron character.

4. The fixation of an unshared electron pair at the nitrogen by the formation of N-oxides leads in practice to the freeing of the nitrogen from the conjugated system and an abrupt change in the optical properties of the molecule.

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THE SPECTROPHOTOMETRIC INVESTIGATION OF DIPHENYLAMINE AND ITS DERIVATIVES IN CONCENTRATED SULFURIC ACID

II. THE ABSORPTION SPECTRA OF DISUBSTITUTED p-HYDROXY AND p-METHOXY DERIVATIVES OF DIPHENYLAMINE

P. M. Bugai

1. Absorption spectra of 4,4'-dihydroxydiphenylamine. 4,4'-Dihydroxydiphenylamine was synthesized by the method described [1] and was then purified to spectrographic purity. Figure 1 and Table 1 give data on the absorption spectra of 4,4'-dihydroxydiphenylamine with different times of standing of a solution of this substance in sulfuric acid. Curve 1, Fig. 1, determined at the moment of dissolving, has a band with an absorption maximum at 276 mμ in the middle ultraviolet and this forms a curve in the neighboring ultraviolet region. In the visible region this curve has a broad band with an absorption maximum at 645 mμ and an absorption minimum at 890 mμ.

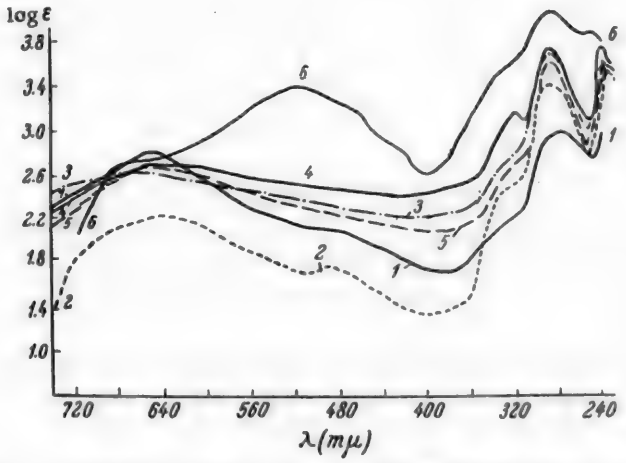


Fig. 1. Absorption spectra of 4,4'-dihydroxydiphenylamine. 1) At the moment of dissolving in H_2SO_4 ($1 \cdot 10^{-3}$ mole); 2) 6 days after dissolving ($1 \cdot 10^{-3}$ mole); 3) after 12 days ($5 \cdot 10^{-4}$ mole); 4) after 30 days ($5 \cdot 10^{-4}$ mole); 5) after 45 days ($5 \cdot 10^{-4}$ mole; 6) in ethanol at the moment of dissolving ($1 \cdot 10^{-4}$ mole).

From the determination of the absorption spectra of the sulfuric acid solution after 6 days we obtained curve 2 which already shows a considerable difference from curve 1. In curve 2 the band with the absorption

maximum in the ultraviolet region is higher as regards the absorption intensity than the similar band of curve 1 and is displaced by 6 mμ into the long-wave region. The curve then has a deflection with its center at 315 mμ, which lies above the corresponding center of the deflection of curve 1. Subsequently this curve, descending below curve 1, forms a deflection at 390-360 mμ, which has already developed into a minimum at 410 mμ. In the visible region, curve 2 forms two further bands with absorption maxima (Fig. 1, Table 1).

TABLE 1

Curve No. in Fig. 1	Concentration (mole) of 4,4'-dihydroxydiphenylamine	Number of days after which the spectrum of the solution was determined	Color of the solution in conc. H_2SO_4	Band order	Maxima of the absorption bands: ε	Maxima of the absorption bands: λ (mμ)	Increase of the intensity of the absorption maxima of the bands above the initial value
1	$1 \cdot 10^{-3}$	At the moment of dissolving	Green-blue	I	977	278	1.0
				II	143—251	330—306	1.0
				III	676	646	1.0
2	$1 \cdot 10^{-3}$	6	The same	I	2692	283	2.7
				II	282—501	330—307	2.0
				IIa	34—25	390—360	1.0
				IIIa	60	493	1.0
				III	174	643	0.3
3	$5 \cdot 10^{-4}$	12	Light green-blue	I	4677	286	4.9
				II	251—794	347—308	3.0
				III	407	650	0.6
4	$5 \cdot 10^{-4}$	30	The same	Ia	4467	234	1.0
				I	5370	286	5.5
				II	1338	320	8.6
				III	501	645	0.74
				IV	33	960 min	1.0
5	$5 \cdot 10^{-4}$	45	The same	Ia	3981	230	0.9
				I	4169	285	4.3
				II	398—703	330—305	3.0
				III	468	644	0.7
				IV	38	960	1.15
6	$1 \cdot 10^{-4}$	At the moment of solution in ethanol	Blue	Ia	7762	246	1.7
				I	12590	281	13.0
				IIIa	2512	514	42.0
				III	447—724	670—660	1.1

Curve 3, Fig. 1 was obtained from the investigation of the solution 12 days after dissolving. This curve rises above curves 2 and 1 and has an unusual shape. In the visible region, curve 3 forms bands with absorption minima at 410 mμ and absorption maxima at 650 mμ. With respect to absorption intensity the maximum lies above the similar maximum of curve 2 and below the maximum of the same band of curve 1.

Here it must be mentioned that the intensity of the blue color of the sulfuric acid solution increases with the time of standing of the solution and when the determination was made it was, therefore, necessary to dilute these solutions.

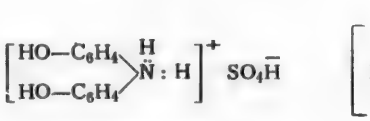
Curve 4 was obtained after 30 days. In the extreme ultraviolet this curve forms a small band with an absorption maximum at 230 mμ. The maximum of band I (286 mμ) of this curve practically coincides with the maxima of band I of curves 3 and 2 and as regards absorption intensity lies above the similar maxima of curves 1 and 3. Subsequently this curve forms a band with an absorption maximum at 320 mμ, which as regards absorption intensity lies above the centers of the deflection of curves 2, 3 and 5. In the visible region curve 4 forms bands with a minimum at 440 mμ and a maximum at 645 mμ. This curve is terminated by another band with an absorption minimum at 960 mμ (this band is not shown in Fig. 1; see Table).

Curve 5, obtained 45 days after the substance was dissolved in sulfuric acid, behaves anomalously compared with the other curves. Almost the entire curve lies below curve 3 as regards absorption intensity but to a considerable extent it duplicates this curve. Like curve 4, at the end of the ultraviolet region curve 5 has a small band Ia with an absorption maximum at the same wavelength but, as regards absorption intensity, it lies below the maximum of the same band of curve 4. Curve 5 is terminated by a broad band with an absorption maximum at 895 mμ and an absorption maximum at 960 mμ (not shown in Fig. 1).

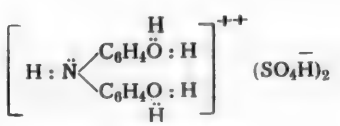
We have included curve 6, obtained for a solution of 4,4'-dihydroxydiphenylamine in ethanol, for purposes of comparison. As regards absorption intensity, curve 6 lies above the other curves and possesses an unusual absorption band. In the extreme ultraviolet it has a small band Ia with an absorption maximum at 246 mμ, which almost completely coincides at this point with the minimum band of curve 1. As regards the wavelengths, the maximum of band I of this curve coincides with the similar maxima of curves 2 and 5 and is somewhat displaced to one or the other side of the maxima of curves 3 and 4. As regards the absorption intensity, the maximum of band I lies above the similar maxima of curves 1, 2, 4 and 5. Curve 6 then forms a broad band with an absorption minimum at 400 mμ, i.e., where the minima of the other curves occur but the absorption intensity is here considerably higher than on the other curves. Further along this curve there is a broad band with an absorption maximum at 516 mμ. In the distant visible region curve 6 forms a deflection with a deflection center at 645 mμ, i.e., where curves 1, 2, 4 and 5 have absorption maxima.

Comparing the curves of the absorption spectra of the sulfuric acid solution with the curve of the ethanol solution it is seen that as a result of the action of concentrated sulfuric acid on the substance, substances changes occur. It must be noted, however, that curve 6, obtained after 45 days, did not show any new feature but, on the contrary, approximated to curve 3 (determined after 12 days). This also is, evidently, not incidental. This curve suggests that in this instance as a result of the chemical reaction of the substance with sulfuric acid a critical moment has occurred, of such a type that the equilibrium was displaced in the reverse direction and approached the previous state, which was expressed by curve 3. The bathochromic displacement of all the curves of the absorption spectra of the sulfuric acid solutions in comparison with the ethanol solution indicates that a considerable change occurs as a result of the reactions of the substance with concentrated sulfuric acid.

As regards the chemism of the reaction of 4,4'-dihydroxydiphenylamine with concentrated sulfuric acid at different periods of reaction of the latter with the substance it must be assumed that very complex processes occur here because sulfuric acid is an oxidizer as well as a salt former. As a result of the formation of salts we can also obtain such compounds as



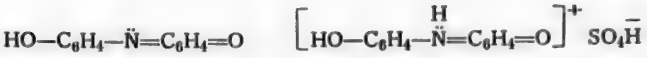
Ammonium salt



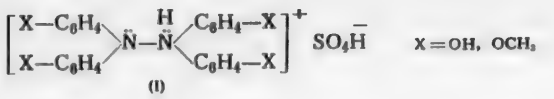
Oxonium salt

All these compounds displace the bands of the absorption spectra somewhat into the long-wave region.

With the presence of two hydroxyl groups in the para position of the substance the oxidation processes can proceed in the most varied manner. An oxidation process of the hydroxyl groups may occur with the formation of indophenol and its salts.



An oxidation process also occurs at the amino groups, as we have previously described for other substances [2], with the formation of an azene ion, which by subsequent condensation with 4,4'-dihydroxydiphenylamine, forms an azene derivative of phenylhydrazine (I).



(I)

With further oxidation, compounds of the quinoid type may be formed which as a result of continuous action by sulfuric acid again form sulfates, no longer of the quinoid type; this also leads to a reduction in the intensity of the absorption bands. It is possible that this also occurred with the solution after standing for 45 days. The possibility of the formation of compounds of the phenazine type also is not excluded, as H. Wieland [3] considers for diphenylamine.

Repeated dilution of the water of colored sulfuric acid solutions of 4,4'-dihydroxydiphenylamine does not lead to hydrolysis and a change in the color of the solutions.

2. Absorption spectra of 4-hydroxy-4'-methoxydiphenylamine. 4-Hydroxy-4'-methoxydiphenylamine was synthesized by a method we developed [4]; the melting point agreed well with literature data.

Figure 2 shows the curves of the absorption spectra of a sulfuric acid solution of 4-hydroxy-4'-methoxydiphenylamine as a function of the time of standing of this solution, and Table 2 gives all the data for these curves. Curve 1 indicates the absorption spectrum of the substance in concentrated sulfuric acid at the moment of solution. This curve is characteristic for 4-hydroxy-4'-methoxydiphenylamine sulfate. It is considerably lower as regards absorption intensity and is displaced into the short-wave region compared with the curve of 4-hydroxy-4'-methoxydiphenylamine in an ethanol solution (curves 1 and 5). Curve 1 has one band with an absorption maximum at 266 mμ.

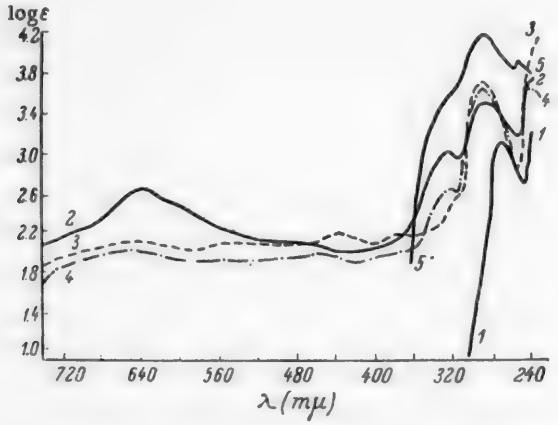


Fig. 2. Absorption spectra of 4-hydroxy-4'-methoxydiphenylamine. 1) At the moment of dissolving in H_2SO_4 ($1 \cdot 10^{-3}$ mole); 2) 8 days after dissolving ($5 \cdot 10^{-4}$ mole); 3) after 17 days ($5 \cdot 10^{-4}$ mole); 4) after 33 days ($5 \cdot 10^{-4}$ mole); 5) in ethanol at the moment of dissolving ($1 \cdot 10^{-4}$ mole).

Curve 2 was obtained after 8 days. This curve is considerably higher as regards absorption intensity and differs markedly in its position from curve 1. A new band with an absorption maximum at 320 mμ was formed in curve 2. The curve then enters far into the visible region and forms two bands with absorption maxima there, one at 630 and the second at 900 mμ. (The latter band is not shown in Fig. 2.) After 8 days under the influence of concentrated sulfuric acid the substance has therefore already undergone a marked change in its electron structure and nature.

TABLE 2

Curve No. in Fig. 2	Concentration (moles) of 4-hydroxy-4'-methoxy-diphenylamine	Number of days after which the spectrum of the solution was determined	Color of the solution in concentrated sulfuric acid	Band order	Maxima of the absorption bands		Increase in the intensity of the absorption maxima above the initial value
					ε	λ (mμ)	
1	$1 \cdot 10^{-3}$	At the moment of dissolving	Colorless	I	1349	267	1.0
2	$5 \cdot 10^{-4}$	8	Light blue	I	3715	281	2.75
				II	1000	320	1.0
				III	447	630	1.0
				IV	26	900	1.0
3	$5 \cdot 10^{-4}$	17	The same	I	5248	286	3.4
				II	447	317	0.45
				IIa	151	430	1.0
				III	135	630	0.3
				IV	24	900 min	0.9
4	$5 \cdot 10^{-4}$	33	The same	I	4786	282	3.5
				II	324—447	330—312	0.4
				IIa	102	442	0.7
				III	107	640	0.24
5	$1 \cdot 10^{-4}$	At the moment of dissolving in ethanol	Colorless	Ia	8318	235	1.0
				I	17380	272	13.0

Moreover, curve 3, obtained after 17 days, forms two bands with absorption maxima in the ultraviolet and then enters far into the visible region, forming during its progress two further bands with absorption maxima at 430 and at 630 mμ. This indicates that as a result of the participation of concentrated sulfuric acid the oxidation process evidently ceases and that subsequently a process of the formation of the sulfates of the oxidized substance takes place, in the manner shown above for 4,4'-dihydroxydiphenylamine.

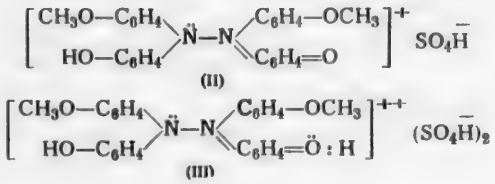
Curve 4 was obtained after 33 days. As may be seen from Fig. 2, this curve differs only slightly from curve 3, evidently because the concentrated sulfuric acid no longer reacts with the substance (curves 3 and 4). In the long-wave region this curve forms two poorly-pronounced bands with absorption maxima at 442 and 640 mμ.

Finally, for purposes of comparison we give curve 5 of the absorption of an ethanol solution of 4-hydroxy-4'-methoxydiphenylamine at the moment in which it was dissolved. This curve is located entirely in the ultraviolet region and encompasses the range of wavelengths of all the previous curves in this region of wavelengths. As regards absorption intensity, curve 5 rises above all the curves and forms two bands with absorption maxima. In its left hand part this curve then shows a considerable deflection which includes the region of the formation of new absorption bands of all the previous curves. In the extreme ultraviolet an absorption maximum of the small band Ia is formed at 235 mμ; similar bands to this do not exist on the curves of the sulfuric acid solution. The maximum of band I of this curve is displaced in the direction of the short waves compared with the analogous maxima of curves 2, 3 and 4 and lies considerably above them as regards absorption intensity.

The fact that there is a hydroxyl group in one of the benzene rings in 4-hydroxy-4'-methoxydiphenylamine and a methoxy group in the other results in this substance being almost colorless (it has a very faint pinkish color) and it differs markedly in this respect from 4,4'-dihydroxydiphenylamine. The high resistance of the molecule of 4-hydroxy-4'-methoxydiphenylamine to the action of concentrated sulfuric acid is also shown by these data.

Taking into consideration the nevertheless considerable variation of the curves of the absorption spectra in a solution of concentrated sulfuric acid and the formation of a deep solution color we can consider that in this instance, as for other substances, oxidation and salt formation reactions take place. Compounds of the azene type (I) are formed here by the same system as we indicated previously in the case of diphenylamine [5].

With further oxidation a quinoid structure of the hydrazine derivative (II) may be formed, and in excess acid, reduction again takes place with the formation this time of a dibasic sulfate (III).



(II)

(III)

Salts are, therefore, formed and this leads to the weakening of the intensity of the absorption bands, which also occurred in the case of the sulfuric acid solution.

3. Absorption spectra of 4,4'-dimethoxydiphenylamine. This substance is interesting in the respect that in contrast to 4,4'-dihydroxydiphenylamine it has methoxy groups in the para position and its molecules cannot, therefore, be oxidized under these conditions.

4,4'-Dimethoxydiphenylamine was obtained by the methylation of 4,4'-dihydroxydiphenylamine with dimethylsulfate.

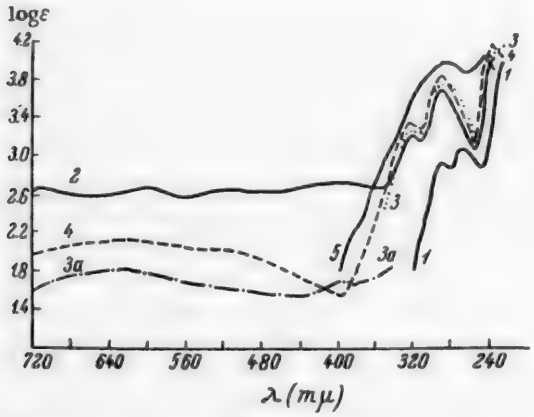


Fig. 3. Absorption spectra of 4,4'-dimethoxydiphenylamine. 1) At the moment of dissolving in H_2SO_4 ($1 \cdot 10^{-4}$ mole); 2) 10 days after dissolving ($1 \cdot 10^{-4}$ mole); 3) after 20 days ($1 \cdot 10^{-4}$ mole); 3a) after 20 days ($1 \cdot 10^{-2}$ mole); 4) after 28 days ($1 \cdot 10^{-4}$ mole); 5) in ethanol at the moment of dissolving ($1 \cdot 10^{-4}$ mole).

Figure 3 shows curves 1-4 of the absorption spectra of 4,4'-dimethoxydiphenylamine in sulfuric acid solution, the curves being obtained for different times of standing. Curve 5 shows the spectrum in an ethanol solution. Curve 1 shows the absorption spectrum of the substance at the moment it was dissolved in concentrated sulfuric acid. As regards absorption intensity this curve is considerably lower than curve 5 and also the other curves. In the ultraviolet region curve 1 has two bands with absorption maxima. Both maxima are near each other and both bands are a continuation of each other.

Curve 2 was obtained after 10 days. It differs considerably from the previous curve. The absorption intensity has increased, the curve has been displaced into the long-wave region and a number of new bands have

TABLE 3

Curve No. in Fig. 3	Concentration (mole) of 4,4'-dimethoxy diphenylamine	Number of days after which the spectrum of the solution was determined	Color of the solution in conc. H_2SO_4	Band order	Maxima of the absorption bands: ε	Maxima of the absorption bands: λ (mμ)	Increase in the intensity of the absorption maxima above the initial value
1	$1 \cdot 10^{-4}$	At the moment of dissolving	Colorless	Ia	1202	267	1.0
				I	832	287	1.0
2	$1 \cdot 10^{-4}$	10	Very faint blue	I	5248	288	6.3
				II	1660	320	1.0
				III	562	398	1.0
				IV	468	595	1.0
				V	468	715	1.0
3	$1 \cdot 10^{-4}$	20	Light blue	I	6026	288	7.2
				II	1778	320	1.06
3a	$1 \cdot 10^{-2}$	20	Intense blue	III	48	396	0.09
				IV	63	620	0.14
4	$1 \cdot 10^{-4}$	28	Light blue	Ia	14130	234	12.0
				I	6457	288	7.8
				II	2239	320	1.35
				III	38	400 min	0.07
				IV	135	610	0.3
5	$1 \cdot 10^{-4}$	At the moment of dissolving in ethanol	Colorless	Ia	10960	246	9.0
				I	10230	283	12.0

been formed in the entire visible region. The new characteristic band II with an absorption maximum at 320 mμ appears in curve 2. Bending sharply, this curve than passes into the visible region and forms three inconspicuous bands there with absorption maxima at 398, 595 and 715 mμ.

Curve 3 which was obtained after the solution had stood for 20 days does not differ substantially from the previous curve. It is very slightly higher as regards absorption intensity and the maxima of both absorption bands are at the same value as for curve 2. In the visible region we determined the values for a $1 \cdot 10^{-2}$ molar solution which had a blue color and obtained curve 3a which has more clearly expressed absorption bands at 396 and 620 mμ.

Curve 4 was obtained after the substance had been dissolved in concentrated sulfuric acid for 28 days. The solution had a bluish color.

As may be seen from Fig. 3, the absorption bands of curves 3 and 4 practically merge in the ultraviolet; in the visible region a broad band with an absorption maximum at 610 mμ is formed.

Finally, an examination of the curve of the ethanol solutions (curve 5) shows that it rises above all the other curves in the ultraviolet region. This curve also has two bands with absorption maxima but they are displaced into the short-wave region with respect to the similar maxima of curves 2-4, and also, to a considerably lesser extent, curve 1.

The process of the oxidation of 4,4'-dimethoxydiphenylamine and its oxidation by sulfuric acid may be represented by the following systems of reactions: the sulfate of this derivative is first formed and it is then oxidized at the nitrogen atom with the formation of an intermediate product, the cation of 4,4'-dimethoxydiphenylhydroxylamine, which is subsequently dehydrated and converted into a cation of the azene type. As a result of the condensation of this cation with dimethoxydiphenylamine a differently colored azene salt of the hydrazine derivative (I) is formed, which can subsequently give a salt and a doubly charged cation.

Since, according to the data of H. Wieland and K. Müller [6], 4,4'-dimethoxydiphenylamine cannot give a benzidine derivative, we consider that our hypothesis of the formation of an azene salt of a hydrazine derivative is correct.

SUMMARY

1. At the moment of dissolving in concentrated sulfuric acid 4-hydroxydiphenylamine and 4,4'dimethoxydiphenylamine form colorless solutions whereas the color of a solution of 4,4'-dihydroxydiphenylamine intensified.

2. After 10-45 days the sulfuric acid solutions of all the substances have a blue or green color and the curves of their absorption spectra indicate the progress of the reaction of the substances with the sulfuric acid to an extent depending on the time of standing of the solution.

3. On the basis of a comparison of our observations with literature data we consider that, being oxidized in concentrated sulfuric acid, all the investigated substances form ions of the azene type. Other oxidation and condensation reactions may then occur with the formation of colored azene products of hydrazine derivatives.

4. The available data indicate the identical character of the chemical reaction of the investigated substances with concentrated sulfuric acid.

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THE SPECTROPHOTOMETRIC INVESTIGATION OF DIPHENYLAMINE AND ITS DERIVATIVES IN CONCENTRATED SULFURIC ACID

III. COMPARISON OF THE ABSORPTION SPECTRA OF VARIOUS p-HYDROXY- AND p-METHOXY DERIVATIVES OF DIPHENYLAMINE

P. M. Bugai

In this work, in order to examine the influence exerted by functional groups in diphenylamine derivatives on the reaction of the substances with concentrated sulfuric acid and the nature of the kinetics and mechanism of the reaction, a comparison is made of the absorption-spectra curves of all the hydroxyl and methoxy derivatives of diphenylamine, substituted in the para positions.

First the absorption-spectra curves of all the substances, obtained at the moment of their solution in concentrated sulfuric acid, are examined. Figure 1 gives the absorption-spectra curves of diphenylamine (curve 1), 4-hydroxydiphenylamine (curve 2), 4-methoxydiphenylamine (curve 3), 4,4'-dihydroxydiphenylamine (curve 4), 4-hydroxy-4'-methoxydiphenylamine (curve 5) and 4,4'-dimethoxydiphenylamine (curve 6). From Fig. 1 it is seen that as regards absorption intensity, curve 1 lies below all the curves and with respect to the position of the absorption maximum of the band it is displaced further than all the others into the ultraviolet region. This is not accidental because diphenylamine shows its maximum capacity for salt formation with concentrated sulfuric acid here. Curve 2 differs markedly in its position from curve 1. It is higher as regards absorption intensity and the absorption maximum is displaced by 31 mμ into the long-wave region (curves 1 and 2 and Table 1). With 4-hydroxydiphenylamine, salt formation at the nitrogen atom is evidently considerably impeded by the influence of the free hydroxyl group and, in addition, by the formation of salts of the oxonium type.

The stabilization of the free hydroxyl group of 4-hydroxydiphenylamine by the conversion of the latter to 4-methoxydiphenylamine leads to the fact that the absorption curve approaches the curve of diphenylamine (Fig. 1, curves 3 and 1). This position of curve 3 indicates that in its properties 4-methoxydiphenylamine closely resembles diphenylamine, i.e., it has a considerable capacity for salt formation.

The introduction of two hydroxyl groups in the para position leads to the appearance of completely different qualities. In the first place, 4,4'-dihydroxydiphenylamine has an intense blue color; secondly, it can react in the most varied manner with sulfuric acid and form salts with it. Curve 4 gives a good illustration of this feature of the substances in concentrated sulfuric acid compared with the other curves in this diagram. In the ultraviolet region curve 4 has a broader absorption band than the previous curves. Curve 4 subsequently enters a considerable way into the visible region, forming another series of bands with absorption minima and maxima.

By closing one of the hydroxyl groups of 4,4'-dihydroxydiphenylamine we convert it into 4-hydroxy-4-methoxydiphenylamine whose absorption spectra curve has a very distinct character. The character of curve 5 duplicates that of curve 3 but rises somewhat above it as regards absorption intensity.

The combination of hydroxyl and methoxy groups in the para position makes the substance colorless and therefore displaces the entire curve into the ultraviolet region and, in addition, makes the substance resemble 4-methoxydiphenylamine and in part 4-hydroxydiphenylamine as regards its chemical properties.

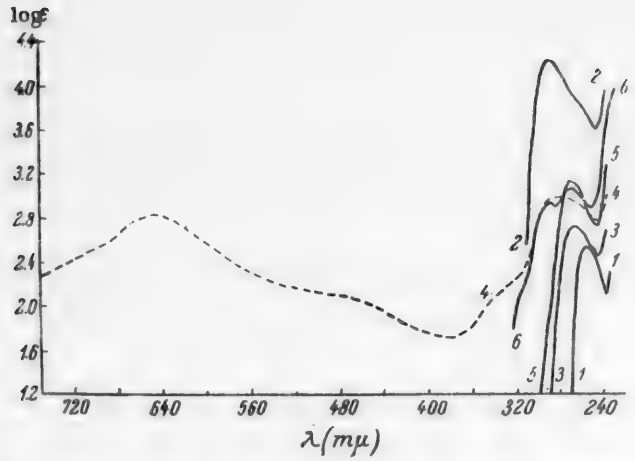

Fig. 1. Absorption spectra of the substances at the moment of dissolving in H_2SO_4. 1) Diphenylamine ($1 \cdot 10^{-3}$ mole); 2) 4-hydroxydiphenylamine ($5 \cdot 10^{-5}$ mole); 3) 4-methoxydiphenylamine ($1 \cdot 10^{-3}$ mole); 4) 4,4'-dihydroxydiphenylamine ($1 \cdot 10^{-3}$ mole); 5) 4-hydroxy-4'-methoxydiphenylamine ($1 \cdot 10^{-3}$ mole); 6) 4,4'-dimethoxydiphenylamine ($1 \cdot 10^{-4}$ mole).

The absorption maximum of band I of curve 6 coincides with respect to wavelength with similar maxima of curves 5 and 2 and the band with an absorption maximum at 286 mμ coincides with the maximum of the band of curve 3 of 4-methoxydiphenylamine.

TABLE 1

Curve No. in Fig. 1	Name of substance	Color of the solution in conc. H_2SO_4	Band order	Maxima of the absorption bands		Increase in intensity of absorption maxima of the bands compared with the absorption band of diphenylamine
				ε	λ (mμ)	
1	Diphenylamine ($1 \cdot 10^{-3}$ mole)	Colorless	Ia	347	254	1.0
2	4-Hydroxy-diphenylamine ($5 \cdot 10^{-5}$ mole)	The same	I	18200	285	52.5
3	4-Methoxydiphenylamine ($1 \cdot 10^{-3}$ mole)	The same	Ia	525	265	1.5
4	4,4'-Dihydroxydiphenylamine ($1 \cdot 10^{-3}$ mole)	Blue	I	977	276	2.8
			II	141—251	330—306	1.0
			III	676	645	1.0
5	4-Hydroxy-4'-methoxydiphenylamine ($1 \cdot 10^{-3}$ mole)	Colorless	Ia	1349	267	4.0
6	4,4'-Dimethoxydiphenylamine ($1 \cdot 10^{-4}$ mole)	The same	Ia	1202	267	3.5
			I	832	286	2.4

Summing up the above it may be said that a hydroxyl group entering the molecule of diphenylamine exerts a substantial influence on the character of the absorption spectrum in sulfuric acid solution. A particularly great influence is exerted by the presence of two hydroxyl groups which completely changes the

nature of the substance and the character of the absorption-spectra curve. Methoxy groups stabilize the molecules of the substance and make their properties close to those of diphenylamine. A substance with mixed groups (hydroxyl and methoxy groups) occupies a rather intermediate position between the methoxy and hydroxyl derivatives of diphenylamine. As regards absorption spectra, the dimethoxy derivative of diphenylamine approximates to 4-hydroxy-4'-methoxydiphenylamine and 4-methoxydiphenylamine.

Figure 2 gives the absorption-spectra curves of derivatives of diphenylamine after 5-12 days under the action of concentrated sulfuric acid. (The data for each curve are given in Table 2; the numbers of the curves are the same as in Fig. 1). When the absorption-spectra curves are compared it is seen that they have much in common. Curves 1 and 3 stand out somewhat against the background of the other curves. The absorption spectrum of curve 1 represents a mixture of diphenylamine salts of the ammonium and azene type. The band in the extreme ultraviolet with an absorption maximum at 254 mμ is characteristic for the first type of salt and the new band II with the absorption maximum at 320 mμ for the second type. Curve 3 shows that 4-methoxydiphenylamine has a lesser capacity for salt formation than diphenylamine and its band I with an absorption maximum at 285 mμ is characteristic for the substance itself, while band II indicates the formation of a new chemical substance.

TABLE 2

Curve No. in Fig. 2	Name of substance	Number of days after which the spectrum of the solution was determined	Color of the solution in conc. H_2SO_4	Band order	Maxima of the absorption bands: ε	Maxima of the absorption bands: λ (mμ)	Increase in the intensity of the absorption maxima of the bands compared with the absorption band of diphenylamine
1	Diphenylamine ($1 \cdot 10^{-3}$ mole)	10	Colorless	I	479	254	1.0
				II	43	320	1.0
2	4-Hydroxydiphenylamine ($5 \cdot 10^{-5}$ mole)	12	Green-blue	I	23440	285	50.0
				II	2512—3981	332—305	72.0
				III	398—501	350—356	1.0
				IV	398	540	1.0
				V	631	700	1.0
3	4-Methoxydiphenylamine ($1 \cdot 10^{-3}$ mole)	5	Colorless	I	1122	285	2.3
				II	62	322	1.4
4	4,4'-Dihydroxydiphenylamine ($5 \cdot 10^{-4}$ mole)	12	Blue	I	4677	286	9.8
				II	251—794	347—308	14.0
				III	151	410 min	0.34
				V	407	650	0.64
5	4-Hydroxy-4-methoxydiphenylamine ($5 \cdot 10^{-4}$ mole)	8	Bluish	I	3715	281	8.0
				II	1000	319	23.0
				III	107	410 min	0.24
				V	447	630	0.7
6	4,4'-Dimethoxydiphenylamine ($1 \cdot 10^{-4}$ mole)	10	Faint blue	I	5248	288	11.0
				II	1660	320	39.0
				III	562	398	1.3
				IV	467	595	1.2
				V	467	715	0.7

The curves obtained (2 and 4) resemble each other in character but curve 2 is higher as regards absorption intensity. Both curves have identical bands with absorption maxima in the ultraviolet and also deflections on the curves in the same region of wavelengths. In the visible region curves 2 and 4 approach each other closely and have the same type of character.

Curves 5 and 6 are also similar in the ultraviolet region. As regards absorption intensity curve 6 lies somewhat higher than curve 5 and the maximum of the absorption band I is displaced by 8 mμ into the short-wave region compared with the similar maximum of curve 5. The maxima of the second absorption bands of both curves are at identical values of the wavelengths and coincide with the similar bands of all the other curves.

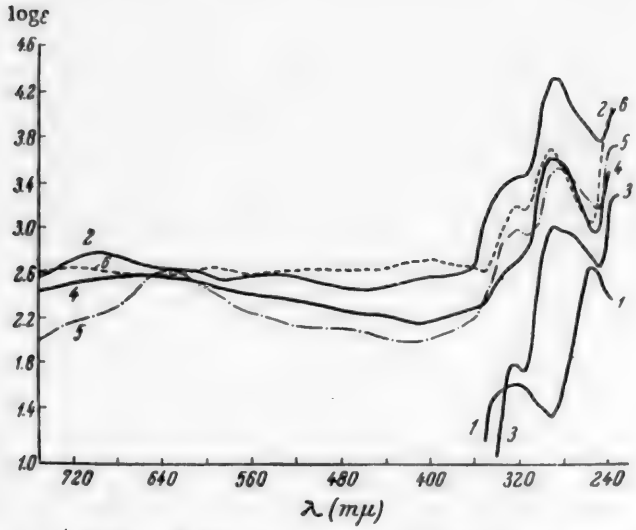

Fig. 2. Absorption spectra of the substances 5-12 days after dissolving in H_2SO_4. 1) Diphenylamine ($1 \cdot 10^{-3}$ mole; 10 days); 2) 4-hydroxydiphenylamine ($5 \cdot 10^{-5}$ mole; 12 days); 3) 4-methoxydiphenylamine ($1 \cdot 10^{-3}$ mole; 5 days); 4) 4,4'-dihydroxydiphenylamine ($5 \cdot 10^{-4}$ mole; 12 days), 5) 4-hydroxy-4-methoxydiphenylamine ($5 \cdot 10^{-4}$ mole; 8 days); 6) 4,4'-dimethoxydiphenylamine ($1 \cdot 10^{-4}$ mole; 10 days).

These curves differ somewhat from each other in the visible region. The minimum of the broad band of curve 5 is under band III with the absorption maximum of curve 6 while the maximum of the band of curve 5 is superposed on curve 6 between two bands with absorption maxima.

Comparing the absorption spectra as a whole it may be said that a considerable change in the substances under the action of concentrated sulfuric acid has already taken place after 5-12 days and chemical compounds of identical character have been formed in all instances. This is indicated by the new bands which appear on the absorption-spectra curves. Here the second bands of all the curves reflect this chemical change as do also the absorption bands formed in the visible region in curves 2, 4, 5 and 6.

We consider that under these conditions salts of the azene type are formed both in the case of diphenylamine and all its derivatives.

In consequence, from the variation in the character of the absorption-spectra curves under these spectrophotometric conditions we can also form a judgment on the influence exerted by concentrated sulfuric acid on these or other substances. Various functional groups exert a considerable influence on the character of the chemical reaction.

Comparing the absorption-spectra curves of hydroxyl and methoxy derivatives of diphenylamine in sulfuric acid solution after 19-33 days it is seen in Fig. 3 that in this instance nearly all the curves extend from the ultraviolet to the extreme visible region and all the solutions have a particular color. The absorption-spectra curves of all the diphenylamine derivatives, determined after the continued action of the acid and represented in Fig. 3, indicate that the character of their absorption spectra is identical.

In the ultraviolet region each of curves 2-6 have two single-type absorption bands. The first bands with absorption maxima are located at practically the same wavelength within the limits of 282-288 mμ for

TABLE 3

Curve No. in Fig. 3	Name of substance	Number of days after which the spectrum of the solution was determined	Color of the solution in conc. H_2SO_4	Band order	Maxima of the absorption bands: ε	Maxima of the absorption bands: λ (mμ)	Increase in the intensity of the absorption maxima of the bands compared with the absorption band of diphenylamine
1	Diphenylamine ($1 \cdot 10^{-3}$ mole)	19	Colorless	Ia	617	254	1.0
				II	190	320	1.0
1a*	Diphenylamine ($1 \cdot 10^{-3}$ mole)	28	Faint blue	Ia	1072	254	1.7
				II	759	318	4.0
				III	100—159	370—352	1.0
2	4-Hydroxydiphenylamine ($5 \cdot 10^{-5}$ mole)	30	Light green	Ia	15850	265—257	26.0
				I	25720	285	1.0
				II	10720	320	57.0
				III	1995—3162	370—344	19.0
				IV	1778	660	1.0
3	4-Methoxydiphenylamine ($1 \cdot 10^{-4}$ mole)	25	Light lilac	I	3162	285	0.12
				II	1259	317	6.6
				III	309	370	3.0
				IV	204	600	0.15
				V	195	710	1.0
4	4,4'-Dihydroxydiphenylamine ($5 \cdot 10^{-4}$ mole)	30	Light blue	Ia	4467	234	7.2
				I	5370	286	0.2
				II	1338	320	7.0
				IV	501	645	0.3
5	4-Hydroxy-4'-methoxydiphenylamine ($5 \cdot 10^{-5}$ mole)	33	The same	I	4786	282	0.18
				II	324—447	330—312	2.1
				III	102	440	0.95
				IV	107	640	0.66
6	4,4'-Dimethoxydiphenylamine ($1 \cdot 10^{-4}$ mole)	28	The same	Ia	14130	233	23.0
				I	6457	288	0.25
				II	2239	320	12.0
				III	38	400 min	0.3
				IV	135	610	0.08

* For data on curves 1b, 1c and 1d see the 1st paper, J. Gen. Chem., 27, 1632 (1957).

the different substances but they are all displaced by 30-40 mμ compared with the similar maxima of diphenylamine curves (see curves 1, 1a and 1d). With regard to absorption intensity the maxima of this band of all the curves of diphenylamine derivatives are located above the similar bands of diphenylamine, except for curves 1b and 1d, but also differ somewhat from each other.

The position of the maxima of the first absorption-spectra bands in all the curves of the diphenylamine derivatives in Fig. 3 indicates that under the conditions of the investigation the usual ammonium type of salt formation is almost absent and the band of the diphenylamine derivative itself appears, which is also characteristic for solutions in ethanol.

The second absorption bands of all the curves of diphenylamine (curve 1b) and of its derivatives are located within the same range of wavelengths – at 317-320 mμ – and at this point, only curve 5 has a band in the form of a deflection at 312-330 mμ, but they differ from each other as regards absorption intensity (see curves 1, 1a and 1d, and also 2-6 and the data in Table 3).

Here it is important to note that in all instances there is a characteristic band, signified in Table 3 by band II, which illustrates the formation of a new azene salt in all the derivatives of diphenylamine. This serves to confirm the single-type character of the chemical reaction proceeding during the oxidation of diphenylamine derivatives with the continued action of concentrated sulfuric acid.

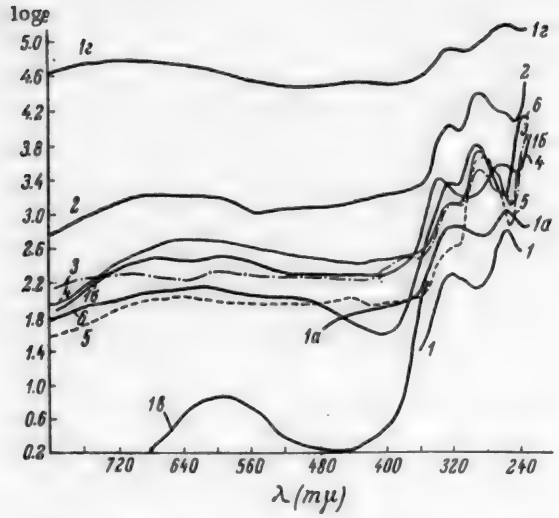

Fig. 3. Absorption spectra 19-33 days after dissolving in H_2SO_4. 1) Diphenylamine ($1 \cdot 10^{-3}$ mole; 19 days); 1a) diphenylamine ($1 \cdot 10^{-3}$ mole; 28 days); 1b) diphenylamine ($1 \cdot 10^{-4}$ mole; the solution was heated for 60 hours, the water was eliminated and the spectrum was determined in concentrated sulfuric acid); 1c) diphenylamine ($1 \cdot 10^{-2}$ mole; the solution was allowed to stand in the cold for 265 days, the product was separated by water and the spectrum was determined in ethanol); 1d) diphenylamine ($1 \cdot 10^{-5}$ mole; it was oxidized with hydrogen peroxide, the precipitate was separated by water and the spectrum was determined in concentrated sulfuric acid); 2) 4-hydroxydiphenylamine ($5 \cdot 10^{-5}$ mole; 30 days); 3) 4-methoxydiphenylamine ($1 \cdot 10^{-4}$ mole; 25 days); 4) 4,4'-dihydroxydiphenylamine ($5 \cdot 10^{-4}$ mole; 30 days); 5) 4-hydroxy-4'-methoxydiphenylamine ($5 \cdot 10^{-5}$ mole; 33 days); 6) 4,4'-dimethoxydiphenylamine ($1 \cdot 10^{-4}$ mole; 28 days).

The formation of absorption bands and the character of all the curves in the visible region also indicate the single-type character of the absorption spectrum and, therefore, the uniformity of the electron structure of all the substances and they show that the deepening of the color also takes place to an approximately similar extent (for the color of the solutions see Table 3).

The functional groups naturally have some influence on the character of the curves and their distribution with regard to absorption intensity. This is clearly illustrated by curve 2 (4-hydroxydiphenylamine) and curves 5 and 6 (4-hydroxy-4'-methoxydiphenylamine and 4,4'-dimethoxydiphenylamine).

The following general formula may also serve to illustrate the single-type character of the chemical reaction

$$\left[\begin{matrix} X-C_6H_4 \\ X'-C_6H_4 \end{matrix}\!\!>\!\ddot{N}\right]^{+} SO_4\bar{H} \qquad X \text{ \& } X' = H,\ OH,\ OCH_3$$

A similar reaction with concentrated sulfuric acid was shown by V. Hückel [1] for phenylhydroxylamine and by us [2].

With more powerful oxidation different condensation of the molecules of diphenylamine derivatives may take place with the formation of azene compounds of the benzidine type; detailed information was given regarding these in our previous communications [3, 4] in the works of Kehrmann and St. Micewicz [5] and Wieland [6, 7].

SUMMARY

1. As a result of the continued action of concentrated sulfuric acid on various hydroxyl and methoxy derivatives of diphenylamine, solutions of uniform color are formed and similar spectra curves are obtained. A considerable similarity of the absorption bands is established but the intensity of the absorption maxima is different.

2. Diphenylamine possesses the greatest activity for salt formation while as a result of the influence of the functional groups other derivatives of diphenylamine have a lesser capacity for the usual salt formation of the ammonium type.

3. The appearance of a second absorption band at 318-329 mμ in the spectrum of diphenylamine and its derivatives and the formation of similar bands in the visible region and, in addition, the character of the color of the solutions all indicate the single-type character of the chemical reaction of the substances with concentrated sulfuric acid and the similar structure of the diphenylamine derivatives.

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DIALKYL AMIDES OF TRIAROXYPHOSPHAZOSULFURIC ACIDS AND AROMATIC ESTERS OF N,N-DIALKYLSULFAMIDO-N'-PHOSPHORIC ACIDS

A. V. Kirsanov and Z. D. Nekrasova

Dialkylamides of triaroxyphosphazosulfuric acids and esters of N,N-dialkylsulfamido-N'-phosphoric acids have not been known hitherto. Their preparation and properties are described in this paper.

Dimethyl- and diethyl amides of triaroxyphosphazosulfuric acids were obtained by the action of the dimethyl amide and trichlorophosphazosulfuric acid (I) and the diethyl amide of trichlorophosphazosulfuric acid (II) [1] on the sodium arylates according to the system

$$R_2NSO_2N{=}PCl_3 + 3NaOAr \rightarrow 3NaCl + R_2NSO_2N{=}P(OAr)_3.$$

Dialkyl amides of triaroxyphosphazosulfuric acids are colorless, comparatively low-melting substances which melt without decomposition; only the diethyl amide of triphenoxyphosphazosulfuric acid is a liquid at room temperature. In general dimethyl amides of triaroxyphosphazosulfuric acids melt above the corresponding diethyl amides, with the exception of the dimethyl amide of tri-p-nitrotriphenoxysulfuric acid which melts below the dimethyl amide. Dialkyl amides of triaroxyphosphazosulfuric acid have a pungent-bitter taste; in the completely pure state they are odorless but after keeping for a short time they acquire a faint odor of the corresponding phenol.

The dialkyl amides of triaroxyphosphazosulfuric acids are chemically neutral substances, very difficultly saponified by water, even when boiled. When boiled with 96% alcohol the dialkyl amides of tri-p-chlorotriphenoxy- and trinitrotriphenoxyphosphazosulfuric acids are saponified. At room temperature the dialkyl amides of trinitrotriphenoxyphosphazosulfuric acids are slowly saponified by solutions of alkali. All the other dialkyl amides of triaroxyphosphazosulfuric acids are only saponified by alkalis when boiled. Saponification by alkali takes place particularly readily in alcoholic or aqueous-alcoholic solutions, which is explained by the solubility of dialkyl amides of triaroxyphosphazosulfuric acids in alcohol (comp. [2]). In all instances saponification takes place readily and with good yields only up to the diaryl esters of N,N-dialkylsulfamido-N'-phosphoric acids (comp. [3]), according to the systems

$$R_2NSO_2N{=}P(OAr)_3 + 2NaOH \rightarrow H_2O + ArONa + R_2NSO_2NNaPO(OAr)_2$$
$$R_2NSO_2N{=}P(OAr)_3 + H_2O \rightarrow ArOH + R_2NSO_2NHPO(OAr)_2$$

Dialkyl amides of triaroxyphosphazosulfuric acids are insoluble in water, readily soluble in acetone, chloroform, dichloroethane, benzene and hot alcohol, more difficultly soluble in carbon tetrachloride and ether, and difficultly soluble or insoluble in petroleum ether. At room temperature the nitro derivatives are difficultly soluble in alcohol, benzene and ether.

The diaryl esters of N,N-dialkylsulfamido-N'-phosphoric acids are colorless or very slightly colored (nitro derivatives) crystalline substances, melting 30-50° above the corresponding dialkyl amides of triaroxyphosphazosulfuric acids (comp. [3]), insoluble in water, readily soluble in chloroform, acetone, dichloroethane, alcohol,

and benzene (except for the nitro derivatives), difficultly soluble in carbon tetrachloride, very difficultly soluble in ether and petroleum ether. Like the diesters of arylsulfonamidophosphoric acids [3] the diaryl esters are monobasic acids, titrated in aqueous solutions to the phenolphthalein end point. Their alkali salts are readily soluble in water, with the exception of salts of the nitrophenyl esters which are comparatively difficultly soluble in water.

The diaryl esters of N,N -dialkylsulfamido-N'-phosphoric acids were also obtained from the diacyl chlorides of N,N-dialkylsulfamido-N'-phosphoric acids (comp. [3]) according to the system

$$R_2NSO_2NHPOCl_2 + 2ArONa \rightarrow 2NaCl + R_2NSO_2NHPO(OAr)_2.$$

The diesters obtained in this manner were found to be identical with the diesters obtained by the saponification of the dialkyl amides of triaroxyphosphazosulfuric acids. The fact that the diaryl esters of N,N -dialkylsulfamido-N'-phosphoric acids are obtained by the two systems proves their structure quite definitely and confirms the structure of the dialkyl amides of triaroxyphosphazosulfuric acids.

EXPERIMENTAL

Dimethyl amide of triphenoxyphosphazosulfuric acid $(CH_3)_2NSO_2N=P(OC_6H_5)_3$ (III). A solution of 0.02 mole of the dimethyl amide of trichlorophosphazosulfuric acid (I) in 50 ml of benzene was added all at once with vigorous stirring to a suspension of finely-ground, carefully dried sodium phenolate (0.06 mole) in 50 ml of benzene. The temperature of the reaction mixture rose rapidly to 40-50°, the precipitate of sodium phenolate disappeared and a slimy percipitate of sodium chloride was formed. To complete the reaction the mixture was boiled with a reflux condenser on a water bath for 30 minutes. On cooling, the sodium chloride was filtered off and the benzene solution was evaporated under vacuum on a water bath. In the residue was an almost colorless oil which crystallized completely when stirred gently with a glass rod. The yield was 7.9 g (91.0%). To remove acid admixtures the product was triturated with 5 ml of a 0.5 N solution of caustic soda, filtered by suction, washed with water, dried and recrystallized from alcohol : it was in the form of colorless prisms; the m. p. was 88-90°.

Found %: N 6.16, 6.32. $C_{20}H_{21}O_5N_2SP$. Calculated %: N 6.48.

Diethyl amide of triphenoxyphosphazosulfuric acid $(C_2H_5)_2NSO_2N=P(OC_6H_5)_3$ (IV). The reaction was carried out in the same way as for (III). When the reaction was completed the benzene solution was washed rapidly at 0° with 5 ml of a 0.5 N solution of caustic soda, quickly dried with sodium sulfate and the benzene was immediately distilled under vacuum, first at room temperature and toward the end at 30°. In the residue, (IV) was in the form of a colorless liquid; the yield was 8.7 g (94.6%).

Found %: N 6.11, 6.14. $C_{22}H_{25}O_5N_2SP$. Calculated %: N 6.09

Dimethyl amide of tri-p-chloro-triphenoxyphosphazosulfuric acid $(CH_3)_2NSO_2N=P(OC_6H_4Cl\text{-}p)_3$ (V). It was necessary to purify the initial p-chlorophenolate by dissolving in ether. The reaction was carried out in the same flask in which the ethereal solution of the p-chlorophenolate was evaporated under vacuum in order to avoid contact of the p-chlorophenolate with moist air. To obtain a good yield it is advantageous to employ about a 10% excess of the p-chlorophenolate. 8.02 g (~ 100%) of (V) was obtained from 0.015 mole of (I) and 0.050 mole of p-chlorophenolate. To purify the substance it was triturated with 5 ml of a 0.5 N solution of caustic soda, filtered rapidly under vacuum, washed with hot water, dried in air and recrystallized from 50 ml of carbon tetrachloride. (V) was in the form of colorless, fine, long prisms; the m. p. was 119-120°.

Found %: N 5.30, 5.26. $C_{20}H_{18}O_5N_2SPCl_3$. Calculated %: N 5.23.

The diethyl amide of tri-p-chlorotriphenoxyphosphazosulfuric acid $(C_2H_5)_2NSO_2N=P(OC_6H_4Cl\text{-}p)_3$ (VI) was obtained in the same way as (V); the yield was 97.0%; after recrystallizing from petroleum ether (6 g in 200 ml) it was in the form of fine, long, flat needles, similar to mica; the m. p. was 113-115°.

Found %: N 5.12, 5.05. $C_{22}H_{22}O_5N_2SPCl_3$. Calculated %: N 4.97.

When boiled with 96% alcohol (V) and (VI) were saponified to the diesters.

Dimethyl amide of tri-o-chlorotriphenoxyphosphazosulfuric acid $(CH_3)_2NSO_2N=P(OC_6H_4Cl\text{-}o)_3$ (VII). When the reaction was carried out in benzene the yields were very low. The o-chlorophenolate was purified in the same way as the p-chlorophenolate (see V). A solution of 0.02 mole of (I) in 100 ml of ether was added to 0.06 mole of o-chlorophenolate. The reaction took place vigorously and the ether boiled. To complete the process the mixture was boiled with a reflux condenser on a water bath for 30 minutes. The reaction mixture was then carefully washed with 10 ml of a 0.5 N solution of caustic soda and 4 times with water, 10 ml each time. The ethereal solution was dried with sodium sulfate and the ether was distilled. In the residue, (VII) was in the form of needles; the yield was 5.52 g (55.2%); after recrystallization from petroleum ether the m. p. was 69-70°.

Found %: N 5.47, 5.31. $C_{20}H_{18}O_5N_2SPCl_3$. Calculated %: N 5.23.

Diethyl amide of tri-o-chlorotriphenoxyphosphazosulfuric acid $(C_2H_5)_2NSO_2N=P(OC_6H_4Cl\text{-}o)_3$ (VIII). This compound was synthesized in the same way as (VII). It was obtained at first in the form of a colorless, oily liquid which was purified by reprecipitating from benzene solution with petroleum ether; the yield was 69.2%. The product crystallized completely (needles) after a month; the m. p. was 40-42°.

Found %: N 4.76, 4.91. $C_{22}H_{22}O_5N_2SPCl_3$. Calculated %: N 4.97.

Dimethyl amide of tri-p-nitrotriphenoxyphosphazosulfuric acid $(CH_3)_2NSO_2N=P(OC_6H_4NO_2\text{-}p)_3$ (IX). 0.06 mole of sodium p-nitrophenolate was carefully dried under vacuum at 140° to constant weight. A solution of 0.02 mole of (I) in 100 ml of benzene was then added with vigorous stirring. The temperature of the mixture rose to 45-50° as a result of the heat of reaction. The main mass of the nitrophenolate entered into the reaction for 30 minutes and the color of the mixture changed from bright orange to dirty yellow. To complete the process the reaction mixture was boiled for 3 hours with a reflux condenser and was filtered boiling to remove the sodium chloride. (IX) was precipitated (10.6 g, 93.5%) from the benzene filtrate on cooling. After recrystallizing from benzene (400 ml) (IX) was in the form of colorless rhombic plates with an m. p. of 144-146°.

Found %: N 12.53, 12.35. $C_{20}H_{18}O_{11}N_5SP$. Calculated %: N 12.37.

The diethyl amide of tri-p-nitrotriphenoxyphosphazosulfuric acid $(C_2H_5)_2NSO_2N=P(OC_6H_4NO_2\text{-}p)_3$ (X), was obtained similarly to (IX), the yield was 92.3%; it crystallized from benzene as fan-shaped concretions of large colorless prisms; the m. p. was 148-150°.

Found %: N 11.71, 11.79. $C_{22}H_{22}O_{11}N_5SP$. Calculated %: N 11.77.

Dimethyl amide of tri-o-nitrophenoxyphosphazosulfuric acid $(CH_3)_2NSO_2N=P(OC_6H_4NO_2\text{-}o)_3$ (XI). When 0.06 mole of carefully dried sodium o-nitrophenolate (comp. IX) was mixed with a solution of 0.02 mole of (I) in 50 ml of benzene at room temperature the reaction did not commence spontaneously but it took place fairly vigorously with slight heating. When boiling had ceased the mixture was heated on a water bath until the precipitate of bright-red phenolate had almost completely disappeared, which required about 1 hour. 150 ml of benzene was then added, the mixture was heated to boiling, filtered without allowing to cool, in order to remove the sodium chloride, and 3/4 of the volume of benzene was distilled off. The product which was precipitated on cooling was filtered by suction, washed with ether to remove the nitrophenol and dried. The yield was 11.2 g (99.1%). To purify the substance it was recrystallized from benzene with activated carbon. (XI) was in the form of thread-like light-yellow crystals; the m. p. was 141-142°.

Found %: N 12.41, 12.39. $C_{20}H_{18}O_{11}N_5SP$. Calculated %: N 12.37.

The diethyl amide of tri-o-nitrotriphenoxyphosphazosulfuric acid $(C_2H_5)_2NSO_2N=P(OC_6H_4NO_2\text{-}o)_3$ (XII) was readily soluble in benzene and after the reaction had been carried out (see XI) and the sodium chloride

filtered, the benzene was distilled off completely. The solid residue was ground and carefully washed with ether. The yield was 10.7 g (90.0%). To purify the product it was recrystallized from a mixture of petroleum ether (b. p. 85-90°) and benzene (1 : 5). (XII) was in the form of light-yellow fine needles; the m. p. was 115-117°.

Found %: N 11.80, 11.78. $C_{22}H_{22}O_{11}N_5SP$. Calculated %: N 11.77.

When boiled with 96% alcohol (IX, X, XI and XII) were saponified to the diesters.

Dimethyl amide of tri-α-naphthoxyphosphazosulfuric acid $(CH_3)_2NSO_2N=P(OC_{10}H_7\text{-}\alpha)_3$ (XIII). 0.21 mole of sodium in the form of fine wire or powder was added to a solution of 0.115 mole of α-naphthol in 200 ml of ether. When the evolution of hydrogen had completely ceased the solution of naphtholate was decanted from the excess sodium and a solution of 0.035 mole of (I) in 50 ml of benzene was gradually added to it. When the vigorous reaction had ceased (after about 30 minutes) the mixture was boiled with a reflux condenser for a further 30 minutes. When the reaction mixture had cooled it was washed twice with a 0.5 N aqueous solution of caustic soda (25 ml each time), twice with water (25 ml each time), the solution was dried with sodium sulfate, filtered, boiled twice with activated carbon and the solvents were distilled under vacuum on a water bath. (XIII) crystallized from alcohol as small colorless cubes and as rectangular plates from carbon tetrachloride; the yield was 14.3 g (70.0%); the m. p. was 123-124°.

Found %: N 4.88, 4.83. $C_{32}H_{27}O_5N_2SP$. Calculated %: N 4.81.

The diethyl amide of tri-α-naphthoxyphosphazosulfuric acid $(C_2H_5)_2NSO_2N=P(OC_{10}H_7\text{-}\alpha)_3$ (XIV) was obtained similarly to (XIII). It was in the form of colorless fine prisms (from alcohol); the yield was 77.0 %; the m. p. was 110-111°.

Found %: N 4.61, 4.64. $C_{34}H_{31}O_5N_2SP$. Calculated %: N 4.59.

Hydrolysis of the dimethyl and diethyl amides of triaroxyphosphazosulfuric acids. Preparation of the diaryl esters of N,N-dialkylsulfamido-N'-phosphoric acids. A mixture of 0.002 mole of the dimethyl and diethyl amides of triaroxyphosphazosulfuric acid (III-XIV), 15 ml of alcohol and 4.0 ml of a 1 N solution of caustic soda was boiled with a reflux condenser fo 1 hour. The alcohol was distilled off under vacuum on a water bath. The aqueous solution of the sodium salt of the diaryl ester of the corresponding dialkylsulfamidophosphoric acid obtained should be completely transparent, which proves that saponification is complete. In some instances (nitro derivatives) the difficultly soluble sodium salts of the diesters may be precipitated from the solution. To obtain the free diesters the solution was acidified with 2.5 ml of 2 N hydrochloric acid. This led to the precipitation of the free diesters either in an immediate crystalline form or as an oil which soon crystallized. If the corresponding phenol was difficultly soluble in water it precipitated together with the diester and had to be removed by washing with a suitable solvent, usually ether.

The nitro derivatives (IX-XII) and p-chlorophenyl derivatives (V and VI) can also be saponified by boiling with a 1 N aqueous solution of caustic soda (examples XXI and XXII) or with 96% alcohol (examples XXIII and XXIV).

The diphenyl ester of N,N-dimethylsulfamido-N'-phosphoric acid $(CH_3)_2NSO_2NHPO(OC_6H_5)_2$ (XV) was recrystallized from benzene; it was in the form of colorless fine prisms, the yield was 94.1% and the m. p. was 143-144°.

Found %: N 7.68. Equiv. 0.991, 0.965. $C_{14}H_{17}O_5N_2SP$. Calculated %: N 7.87. Equiv. 1.000.

The diphenyl ester of N,N-diethylsulfamido-N'-phosphoric acid $(C_2H_5)_2NSO_2NHPO(OC_6H_5)_2$ (XVI) was recrystallized from petroleum ether as large needles; the yield was 91.0%, the m. p. was 122-123°.

Found %: N 7.31, 7.33. Equiv. 1.005, 0.995. $C_{16}H_{21}O_5N_2SP$. Calculated %: N 7.29. Equiv. 1.000.

The di-p-chlorodiphenyl ester of N,N-dimethylsulfamido-N'-phosphoric acid $(CH_3)_2NSO_2NHPO(OC_6H_4Cl\text{-}p)_2$ (XVII) was recrystallized from carbon tetrachloride as aggregates of small snowflakelike needles. The yield was 70%; the m. p. was 167-168°.

Found %: N 6.39, 6.48. Equiv. 0.996, 0.921. $C_{14}H_{15}O_5N_2SPCl_2$. Calculated %: N 6.58. Equiv. 1.000.

The di-p-chlorodiphenyl ester of N,N-diethylsulfamido-N'-phosphoric acid $(C_2H_5)_2NSO_2NHPO(OC_6H_4Cl\text{-}p)_2$ (XVIII) was recrystallized from petroleum ether as small needles; the yield was 63.0%, the m. p. was 110-112°.

Found %: N 6.09. Equiv. 1.010, 1.020. $C_{16}H_{19}O_5N_2SPCl_2$. Calculated %: N 6.18. Equiv. 1.000.

(XVII) and (XVIII) could also be obtained from (V) and (VI) by boiling with 96% alcohol without the addition of alkali.

The di-o-chlorodiphenyl ester of N,N-dimethylsulfamido-N'-phosphoric acid $(CH_3)_2NSO_2NHPO(OC_6H_4Cl\text{-}o)$ (XIX) was obtained by washing the crude product with boiling water and recrystallizing from benzene (1 g in 15 ml); it was in the form of plates, the yield was 86.0% and the m. p. was 137-139°.

Found %: N 6.52, 6.42. Equiv. 0.985, 1.005. $C_{14}H_{15}O_5N_2SPCl_2$. Calculated %: N 6.58. Equiv. 1.000.

The di-o-chlorodiphenyl ester of N,N-diethylsulfamido-N'-phosphoric acid $(C_2H_5)_2NSO_2NHPO(OC_6H_4Cl\text{-}o)_2$ (XX) was obtained by washing the crude product with boiling water and recrystallizing from petroleum ether (3 g from 150 ml); it was in the form of aggregates of transparent needles shaped like feathers; the yield was 83.7%, the m. p. was 110-111°,

Found %: N 6.10, 6.14. Equiv. 0.996, 0.951. $C_{16}H_{19}O_5N_2SPCl_2$. Calculated %: N 6.18. Equiv. 1.000.

Di-p-nitrodiphenyl ester of N,N-dimethylsulfamido-N'-phosphoric acid $(CH_3)_2NSO_2NHPO(OC_6H_4NO_2\text{-}p)_2$ (XXI). A mixture of 0.002 mole of (IX) in 4 ml of a 1 N solution of caustic soda was boiled with a reflux condenser for 15 minutes, 2.5 ml of 2 N hydrochloric acid was added, the precipitate was filtered by suction, washed with water and ether to remove the p-nitrophenol and recrystallized from alcohol: it was in the form of light-yellow prisms, the yield was 97.5%, the m. p. was 197-198°.

Found %: N 12.55, 12.58. $C_{14}H_{15}O_9N_4SP$. Calculated %: N 12.56.

Di-p-nitrodiphenyl ester of N,N-diethylsulfamido-N'-phosphoric acid $(C_2H_5)_2NSO_2HPO(OC_6H_4NO_2\text{-}p)_2$ (XXII). This was obtained similarly to (XXI); it was recrystallized from alcohol. It was in the form of large, long, light-yellow needles; the yield was 94.4%, the m. p. was 148-150°.

Found %: N 11.92, 11.89. $C_{16}H_{19}O_9N_4SP$. Calculated %: N 11.82.

The sodium salts of (XXI) and (XXII) were comparatively difficultly soluble in cold water.

Di-o-nitrodiphenyl ester of N,N-dimethylsulfamido-N'-phosphoric acid $(CH_3)_2NSO_2NH(OC_6H_4NO_2\text{-}o)_2$ (XXIII). A mixture of 0.002 mole of (XI) and 5 ml of alcohol was boiled with a reflux condenser for 15 minutes, the alcohol was evaporated under vacuum to dryness, the solid residue was washed with ether (removal of nitrophenol) and crystallized from alcohol. (XXIII) was in the form of light-yellow rhombic crystals; the yield was 95.4%, the m. p. was 163-164°.

Found %: N 12.57, 12.60. $C_{14}H_{15}O_9N_4SP$. Calculated %: N 12.56.

Di-o-nitrodiphenyl ester of N,N-diethylsulfamido-N'-phosphoric acid $(C_2H_5)_2NSO_2NH(OC_6H_4NO_2\text{-}o)_2$ (XXIV). It was obtained in the same way as (XXIII); it was recrystallized from alcohol. It was in the form of light-yellow rhombic crystals; the yield was 97.0%, the m. p. was 142-143°.

Found %: N 11.84, 11.84. $C_{16}H_{19}O_9N_4SP$. Calculated %: N 11.82.

The di-α-naphthyl ester of N,N-dimethylsulfamido-N'-phosphoric acid $(CH_3)_2NSO_2NHPO(OC_{10}H_7\text{-}\alpha)_2$ (XXV) was obtained by the general method. The crude product was extracted with chloroform, the solvent was evaporated under vacuum and the residue was carefully washed with ether and recrystallized from alcohol. (XXV) was a finely-crystalline powder; the yield was 92.1%, the m. p. was 190-191°.

Found %: N 6.16. Equiv. 1.001, 0.999. $C_{22}H_{21}O_5N_2SP$. Calculated %: N 6.12. Equiv. 1.000.

Di-α-naphthyl ester of N,N-diethylsulfamido-N'-phosphoric acid $(C_2H_5)_2NSO_2NHPO(OC_{10}H_7\text{-}\alpha)_2$ (XXVI). It was obtained in a similar manner to (XXV) and recrystallized from benzene. It was finely-crystalline powder; the yield was 94.3%, the m. p. was 171-172°.

Found %: N 5.84. Equiv. 0.998, 1.004. $C_{24}H_{29}O_5N_2SP$. Calculated %: N 5.79. Equiv. 1.000.

Preparation of diaryl esters of N,N-dialkylsulfamido-N'-phosphoric acids by the action of sodium arylates on the diacyl chlorides of N,N-dialkylsulfamido-N'-phosphoric acids. 0.02 mole of the corresponding diacyl chloride was dissolved in 20 ml of dry benzene and 0.06 mole of dry, carefully dried and ground phenolate was added with vigorous stirring. The reaction took place vigorously and the mixture became very hot or boiled. To complete the process the mixture was boiled with a reflux condenser for 15-20 minutes, the solvent was then evaporated under vacuum on a water bath, the residue was dissolved in water, the solution was acidified and the precipitated product was filtered by suction, washed, dried and recrystallized. The following compounds were obtained in this manner: (XV), yield 99.7%; (XVI), yield 89.8%; (XVII), yield 75.0%; (XVIII), yield 73.5%. The diesters prepared in this way were found to be identical with the diesters obtained by the hydrolysis of the corresponding N,N-dialkyl amides of triaroxyphosphazosulfuric acids.

SUMMARY

A number of dialkyl amides of triaroxyphosphazosulfuric acids and diaryl esters of N,N-dialkylsulfamido-N'-phosphoric acids were obtained and described.

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TRICHLOROPHOSPHAZO ACYLS, TRICHLOROISOPHOSPHAZO ACYLS AND THEIR DERIVATIVES

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As was recently shown [1], as a result of the action of phosphorus pentachloride on amides of carboxylic acids, trichlorophosphazo acyls of the type $RCON{=}PCl_3$ are obtained; as a result of partial hydrolysis the latter give diacyl chlorides of acylamidophosphoric acids of the type $RCONHPOCl_2$ [2]. When acted on by phosphorus pentachloride the diacyl chloride of trichloroacetylamidophosphoric acid, $CCl_3CONHPOCl_2$, gives the diacyl chloride of the N-phosphoric acid of trichloroimidoacetyl chloride, $CCl_3C(=NPOCl_2)Cl$ [3]. For the sake of brevity, compounds of the type $RC(=NPOCl_2)Cl$ will subsequently be referred to as trichloroisophosphazo acyls since they are isomeric with trichlorophosphazo acyls of the type $RCON{=}PCl_3$ and are closely associated with them genetically, while esters of the type $RC[=NPO(OR')2]OR'$ will be termed triaroxyisophosphazo acyls since they are isomeric with triaroxyphosphazo acyls of the type $RCON{=}P(OR'')_3$.

$RCON{=}P{\equiv}$	$RC{=}NPO$
Phosphazo acyl compounds	Isophosphazo acyl compounds

Until now only one trichloroisophosphazo acyl, namely trichloroisophosphazotrichloro acetyl and certain triaroxyisophosphazo acyls [3] corresponding to it have been known. It is of undoubted interest to determine whether trichloroisophosphazo acyls and triaroxyisophosphazo acyls of other types of carboxylic acids exist or whether trichloroisophosphazo acyls are only stable in the case of trichloroacetic acid and its analogs, a possibility which cannot be excluded because phosphazo compounds derived from trichloroacetamide are incomparably more stable than phosphazo compounds derived from amides of aromatic acids [3].

The amides of triphenylacetic, diphenylchloroacetic and p-nitrobenzoic acids were chosen as the first objects of the investigation. They all give the corresponding trichlorophosphazo compounds, trichlorophosphazodiphenylchloro acetyl $(C_6H_5)_2CClCON{=}PCl_3$ (I) resembling in its properties the derivative of trichloro acetyl ($CCl_3CON{=}PCl_3$), although it decomposes with the evolution of phosphorus oxychloride and the formation of a nitrile somewhat more readily and at a lower temperature (195-200°). Markedly different to it in its properties is trichlorophosphazotriphenyl acetyl $(C_6H_5)_3CCON{=}PCl_3$ (II) which decomposes at the melting point (123-125°), i.e., just as readily and perhaps somewhat more readily than trichlorophosphazo acyls of the aromatic series [1]. Trichlorophosphazo-p-nitrobenzoyl (III), previously described [2], is considerably less stable than (I) but rather more stable than (II) (see below). The following conclusion may therefore be drawn: trichlorophosphazotriaryl acetyls split up on heating into phosphorus oxychloride and the corresponding nitriles just as readily as trichlorophosphazo acyls of the aromatic series but the substitution of even one aryl by chlorine makes trichlorophosphazo acyls almost as stable with respect to thermal dissociation as the phosphazo compound from trichloroacetamide.

By the action of formic acid all three trichlorophosphazo compounds (I, II, III) give the diacyl chlorides of the corresponding acylaminophosphoric acids which also differ from each other markedly with respect to chemical properties. The diacyl chloride of diphenylchloroacetylamidophosphoric acid $(C_6H_5)_2CClCONHPOCl_2$ (IV) already obtained by V. Steinkopf [4] is a stable crystalline substance and by the action of phosphorus

pentachloride gives a good yield of crystalline trichloroisophosphazodiphenylchloro acetyl $(C_6H_5)_2CClC(=NPOCl_2)Cl$ (V), which when acted on by formic acid does not regenerate the diacyl chloride, probably as a result of the presence of a mobile chlorine atom at the carbon of the acetyl group (see below the saponification of the corresponding trinaphthyl ester).

The diacyl chloride of triphenylacetylamidophosphoric acid $(C_6H_5)_3CCONHPOCl_2$ (VI) decomposes completely into triphenylacetonitrile and phosphorus oxychloride at the melting point (128-130°) and it is, therefore, not possible to obtain the corresponding trichloroisophosphazo compound from it. The thermal decomposition evidently proceeds at a lower temperature than the reaction with phosphorus pentachloride.

The diacyl chloride of p-nitrobenzoylamidophosphoric acid (VII) decomposes far more readily than (IV) but more difficultly than (VI). It is therefore possible to obtain a good yield of trichloroisophosphazo-p-nitrobenzoyl $p\text{-}NO_2C_6H_4C(=NPOCl_2)Cl$ (VIII) but it was not possible to regenerate the dichloride (VII) from it by the action of formic acid or water and in all instances, under the most varied reaction conditions, p-nitrobenzoylnitrile is quantitatively formed.

With 3 molecules of sodium α-naphtholate, (I) gives the crystalline trinaphthyl ester $(C_6H_5)_2CClCON=P(OC_{10}H_7\text{-}\alpha)_3$ (IX) which when boiled with water replaces the chlorine by hydroxyl and gives a crystalline triester with the structure $(C_6H_5)_2C(OH)CON=P(OC_{10}H_7\text{-}\alpha)_3$ (X). When the latter is boiled for a longer period with water or an aqueous solution of alkali it gives products from which it was not possible to isolate individual substances. (X) does not contain halogen, does not possess acid properties and is insoluble in alkali. Its phosphorus content corresponds to the proposed composition. Its structure cannot, however, be considered as definitely proven because it is quite unintelligible why hydrolysis of one naphthyl group does not occur simultaneously with the replacement of chlorine by hydroxyl when alkali acts on (IX).

With the α-naphtholate, (V) gives the vitreous triester $(C_6H_5)_2CClC[=NPO(OC_{10}H_7\text{-}\alpha)_2](OC_{10}H_7\text{-}\alpha)$ (XI), which gradually becomes tarry when kept in air and gives only tarry products when saponified with water or alkali.

The diester $(C_6H_5)_2CClCONHPO(OC_{10}H_7\text{-}\alpha)_2$ (XII) was obtained by the usual method [5] from the corresponding dichloride and sodium α-naphtholate; it was a stable crystalline substance. This ester is, therefore, not an intermediate product in the hydrolysis of the esters (IX) and (XI). In the first place the chlorine at the α-carbon atom is evidently hydrolyzed and tarry products are then formed.

When acted on by sodium naphtholate, (III) and (VIII) give the corresponding crystalline triesters: $p\text{-}NO_2C_6H_4CON=P(OC_{10}H_7\text{-}\alpha)_3$ (XIII) and $p\text{-}NO_2C_6H_4C[=NPO(OC_{10}H_7\text{-}\alpha)_2](OC_{10}H_7\text{-}\alpha)$ (XIV).

All the triaroxyisophosphazo acyls hitherto known are vitreous substances [3], (XIV) is therefore the first crystalline triaroxyisophosphazo acyl. With partial hydrolysis by water or by the action of alkali the isomeric esters (XIII) and (XIV) give the same diester $p\text{-}NO_2C_6H_4CONHPO(OC_{10}H_7\text{-}\alpha)_2$ (XV), which together with the method of preparation definitely proves their structure.

It may, therefore, be considered as proven that trichloroisophosphazo acyls $RC(=NPOCl_2)Cl$ and triaroxyisophosphazo acyls $RC[=NPO(OR')_2](OR')$ exist not only in the case of trichloroacetic acid and its analogs but also for aromatic acids with electronegative substituents and for diarylchloroacetic acids. Trichloroisophosphazo acyls and triaroxyisophosphazo acyls from amides of triarylacetic acids cannot, evidently, be obtained under usual conditions because the corresponding trichlorophosphazotriaryl acetyls and diacyl chlorides of triarylacetylamidophosphoric acids are insufficiently stable in the thermal respect.

EXPERIMENTAL

All operations with acyl chlorides and triesters must be carried out in such a way that, as far as possible, the substances and the reaction mixtures do not come into contact with moist air.

Trichlorophosphazodiphenylchloro acetyl (I). A mixture of 1 mole of diphenylchloroacetamide and 0.105 mole of phosphorus pentachloride was heated on an oil bath at 85-95° until the evolution of hydrogen chloride had completely ceased, which required 20-25 minutes. 5 ml of petroleum ether was added to the reaction product (an almost colorless liquid) and the mixture was left to stand for a day at 0°. The completely crystallized substance was ground and filtered, by suction the solid product was washed twice with 2 ml of petroleum ether each time and dried under vacuum. The yield was 94.0%. To purify the substance it was recrys-

tallized from petroleum ether. (I) was in the form of colorless prisms, readily soluble in ether, benzene and carbon tetrachloride, difficultly soluble in petroleum ether; the m. p. was 60-62°. It hydrolyzed slowly when kept in air and reacted readily with water, alcohols and amines.

Found %: P 8.31; Cl 37.10. Equiv. after hydrolysis at 20° 4.98, when boiled 6.02. $C_{14}H_{10}ONPCl_4$. Calculated %: P 8.35; Cl 37.27. Equiv. after hydrolysis at 20° 5.00, when boiled 6.00.

The thermal dissociation of (I) was carried out in the following manner: 0.035 mole of (I) was placed in a 50 ml Claisen flask equipped with two thermometers, the bulb of one of which was immersed in the substance, the bulb of the other being located in the vapor. The substance was heated gradually on an oil bath. Decomposition began at 195° and was completed after 20 minutes at a temperature of 195-200°; 90.0% of the phosphorus oxychloride distilled over during this period. The residue which was an almost colorless liquid was distilled under vacuum, the thermometer with its bulb immersed in the substance being first replaced by a capillary. Almost the entire product distilled at 165-166° at 5 mm; it was a colorless liquid with an unpleasant odor. The yield of diphenylchloroacetonitrile was 91.8%.

Found %: N 6.01. $C_{14}H_{10}NCl$. Calculated %: N 6.18.

When boiled with alkali the diphenylchloroacetonitrile gave benzophenone, which corresponds with literature data [6].

Trichlorophosphazotriphenyl acetyl (II). The reaction was carried out in the same way as for (I) but 30 ml of carbon tetrachloride per 0.03 mole of the reacting substances was added to the reaction mixture. When the reaction was completed the solution was filtered, the carbon tetrachloride was distilled under vacuum at 30-40° and the solid crystalline residue (yield 98.8%) was crystallized from a small amount of carbon tetrachloride or from petroleum ether. (II) was in the form of colorless prisms with an m. p. of 123-125°; it was readily soluble in ether and acetone, more difficultly soluble in carbon tetrachloride and petroleum ether. When melted it decomposed completely into triphenylacetonitrile and phosphorus oxychloride.

Found %: P 7.67; Cl 25.3. Equiv. after hydrolysis 4.75. $C_{20}H_{15}ONPCl_3$. Calculated %: P 7.34; Cl 25.3. Equiv. after hydrolysis 5.00.

Diacyl chloride of diphenylchloroacetylamidophosphoric acid (IV). 0.05 mole of anhydrous formic acid was added to a solution of 0.05 mole of (I) in 15 ml of benzene. A vigorous reaction commenced almost immediately. After 24 hours the crystals – large rectangular prisms – which were precipitated were filtered by suction, washed twice, 3 ml each time, with petroleum ether and dried under vacuum. The mother liquor was evaporated under vacuum to 1/3 its volume and the crystals precipitated were filtered by suction. The total yield was 99.4%, the m. p. was 122-123°, which corresponds to literature data [4].

Trichloroisophosphazodiphenylchloro acetyl (V). A mixture of 0.03 mole of (IV) and 0.03 mole of phosphorus pentachloride was heated with a reflux condenser on an oil bath at 135-140° for 15-20 minutes. During this process 93.0% of the theoretical amount of hydrogen chloride was liberated; the residue [a mixture of phosphorus oxychloride and (V)] was 100%. The phosphorus oxychloride was distilled under vacuum at 40-50°, 1.0 ml of petroleum ether was added to the liquid residue and the mixture was left to stand at 0°. The solidified mass was ground, filtered by suction, the crystalline product was washed twice, 2 ml each time, with petroleum ether and then dried under vacuum. The yield was 87.7%. To purify the substance it was crystallized from petroleum ether (concretions of prisms). (V) was a colorless crystalline substance, readily soluble in almost all the usual organic solvents, difficultly soluble in petroleum ether; the m. p. was 81-83°.

Found %: P 8.79; Cl 37.35. Equiv. after hydrolysis 6.05, 5.93. $C_{14}H_{10}ONPCl_4$. Calculated %: P 8.35; Cl 37.27. Equiv. after hydrolysis 6.00.

Diacyl chloride of triphenylacetylamidophosphoric acid (VI). This was obtained in the same way as (IV) but carbon tetrachloride (50 ml per 0.105 mole) was used instead of benzene as the solvent. After 24 hours the precipitated substance was filtered by suction, washed twice with carbon tetrachloride (2 ml each time) and dried under vacuum; the yield was 98.0%. (VI) was a colorless, crystalline substance (prisms) with an m. p. of 128-130°; it was readily soluble in benzene and acetone and almost insoluble in carbon tetrachloride and petroleum ether.

Found %: N 3.50; Cl 17.55. Equiv. after hydrolysis 3.02. $C_{20}H_{16}O_2NPCl_2$. Calculated %: N 3.48; Cl 18.10. Equiv. after hydrolysis 3.00.

The fusion of (VI) was accompanied by complete dissociation into metaphosphoric acid, phosphorus oxychloride and triphenylacetonitrile. When (VI) was heated with phosphorus pentachloride either no reaction occurred or (at a higher temperature) dissociation took place with the formation of triphenylacetonitrile.

It was not possible to obtain the free acid from (VI) or from (II) by the action of formic acid. In both instances a mixture of the amide and unreacted (VI) was obtained.

Trichloroisophosphazo-p-nitrobenzoyl (VIII). A mixture of 0.05 mole of the diacyl chloride of p-nitrobenzoylamidophosphoric acid (VII) [2] and 0.0525 mole of phosphorus pentachloride was heated on an oil bath at 125-130° until the evolution of hydrogen chloride had completely ceased, which required 20-25 minutes. During this time 98.2% of the theoretical amount of hydrogen chloride was liberated. The phosphorus oxychloride was distilled off under vacuum at 50°. The residue, a faintly colored liquid, crystallized completely when stirred gently with a glass rod. The yield of the crude product was 100.0%. To purify the substance it was recrystallized from 80 ml of a mixture of benzene and petroleum ether (1 : 1), filtered by suction and washed twice (2 ml each time) with petroleum ether. (VIII) was in the form of concretions of colorless prisms; the yield of the pure product was 76.0%, the m. p. was 121-124°; it was readily soluble in benzene, more difficultly soluble in carbon tetrachloride, ether and petroleum ether.

Found %: P 10.25; Cl 35.52. Equiv. after hydrolysis 4.93. $C_7H_4O_3N_2PCl_3$. Calculated %: P 10.30; Cl 35.60. Equiv. after hydrolysis 5.00.

The hydrolysis of (VIII) was carried out in a solution of benzene and carbon tetrachloride by the action of formic acid, in a solution of acetone by the action of water and in a benzene solution by the action of water vapor; in all instances p-nitrobenzonitrile was quantitatively liberated. It was not possible to isolate (VII).

Tri-α-naphthoxyphosphazodiphenylchloro acetyl (IX). 0.03 mole of sodium α-naphtholate in 20 ml of ether was added with stirring to a solution of 0.01 mole of (I) in 20 ml of ether. A fairly vigorous reaction commenced immediately and continued for 15-20 minutes. To complete the reaction the mixture was boiled with a reflux condenser for 15-20 minutes, the precipitated sodium chloride was filtered by suction and the ethereal solution was evaporated to dryness under vacuum. (IX) was contained in the residue in the form of a compact crystalline substance. To purify the product it was recrystallized from 25 ml of a mixture of benzene and petroleum ether (1 : 1), the yield was 57.2 %, the m. p. was 121-122°. (IX) was in the form of colorless plates; it was readily soluble in benzene and acetone, difficultly soluble in carbon tetrachloride, petroleum ether and alcohol.

Found %: N 1.99. $C_{44}H_{31}O_4NPCl$. Calculated %: N 1.98.

Tri-α-naphthoxyphosphazodiphenylhydroxy acetyl (X). A mixture of 0.0015 mole of (IX) in 20.0 ml of water was boiled with reflux condenser for 8 minutes. The residue was converted to drops of oil which on cooling and stirring gently with a glass rod soon crystallized. The precipitate was filtered and washed with water. 0.00151 equiv. of hydrogen chloride was back-titrated in the filtrate. The precipitate was washed with alcohol and dried. (X) was a finely-crystalline powder; the yield was 84.2%, the m. p. was 140-141°. It did not have acid properties and did not titrate with alkali in alcoholic solution. (X) was also obtained by heating (IX) in alcoholic solution with 1 equiv. of alkali.

Found %: P 4.33. $C_{44}H_{32}O_5NP$. Calculated %: P 4.52.

When (X) was heated with a solution of alkali or when it was boiled for a long time with water, tarry products were formed from which individual substances could not be obtained.

Tri-α-naphthoxyisophosphazodiphenylchloro acetyl (XI). The reaction was carried out as for (IX). When the reaction was completed the mixture was cooled to 0° and the ethereal solution was washed with 30.0 ml

of a 0.3 N solution of caustic soda, mixed with ice. The ethereal solution was immediately separated and filtered through two adjacent funnels with filters, in each of which was placed 5.0 g of dry, ground sodium sulfate; the ether was immediately distilled off under vacuum, first at 0°, then at 10°. (XI) was contained in the residue in the form of a vitreous, almost colorless, easily ground substance, readily soluble in acetone, difficultly soluble in benzene and carbon tetrachloride and insoluble in alcohol. The yield was 49.7%, the m. p. 42-47°.

Found %: N 1.97. $C_{44}H_{31}O_4NPCl$. Calculated %: N 1.98.

When (XI) was hydrolyzed by the action of water or alkali in alcoholic solution, tarry products were obtained from which individual substances could not be isolated.

Di-α-naphthyl ester of diphenylchloroacetylamidophosphoric acid (XII). A solution of 0.045 mole of sodium naphtholate in 40 ml of ether was added with stirring to a solution of 0.015 mole of (IV) in 25 ml of ether. When the rather vigorous reaction had ceased the mixture was boiled, the sodium chloride was filtered, the solution was evaporated to a small volume, the precipitated crystals were filtered by suction and they were washed in succession with 1 N hydrochloric acid, water, and alcohol. (XII) was a colorless finely-crystalline powder, readily soluble in aqueous solutions of alkalis with the formation of salts. The yield was 69.4%, the m. p. was 168-170°.

Found %: N 2.17. Equiv. 1.01. $C_{34}H_{25}O_4NP$. Calculated %: N 2.43. Equiv. 1.00.

Tri-α-naphthoxyphosphazo-p-nitrobenzoyl (XIII). The reaction was carried out in the same way as for (IX) but 0.06 mole of the α-naphtholate was dissolved in 60 ml of ether and 0.02 mole of trichlorophosphazo-p-nitrobenzoyl (III) [2] in 60 ml of benzene. After the sodium chloride had been filtered off the solvents were evaporated under vacuum (to avoid contamination by atmospheric moisture). (XIII) was present in the residue in the form of a vitreous, almost colorless, transparent, brittle mass, which crystallized out completely on long standing under petroleum ether. (XIII) was very readily soluble in the usual organic solvents with the exception of petroleum ether; the m. p. was 83-86°, the yield was 99.8%.

Found %: N 4.35. $C_{37}H_{25}O_6N_2P$. Calculated %: N 4.48.

When boiled with alcohol (XIII) was converted to a crystalline substance with an m. p. of 140-143°, the nature of which has not yet been established.

Tri-α-naphthoxyisophosphazo-p-nitrobenzene (XIV). A solution of 0.06 mole of sodium α-naphtholate in 70 ml of ether was added with stirring to a solution of 0.02 mole of (VIII) in 70 ml of benzene. After the rather vigorous reaction had ceased the mixture was boiled with a reflux condenser for 20 minutes. The mixture was then cooled to 0°, washed with 40 ml of a 1 N solution of caustic soda, mixed with ice, the benzene-ether layer was quickly separated and immediately filtered through two adjacent filters each containing 5.0 g of anhydrous sodium sulfate. The filtrate was slowly evaporated under vacuum, first at room temperature, then at 25-30°. (XIV) was present in the residue as a compact crystalline mass. After recrystallization from absolute alcohol, (XIV) was in the form of transparent plates, the m. p. was 147-148°, the yield was 16.5%. The low yield is explained by the fact that during washing, a considerable part of (XIV) was hydrolyzed to (XV), which can be obtained by oxidation of the alkaline solution. (XIV) was fairly readily soluble in ether and chloroform, more difficultly soluble in alcohol and benzene.

Found %: N 4.40. $C_{37}H_{25}O_6N_2P$. Calculated %: N 4.48.

Di-α-naphthyl ester of p-nitrobenzoylamidophosphoric acid (XV) A. Saponification of (XIII). A mixture of 100.0 ml of alcohol, 15.0 ml of a 0.2 N solution of caustic soda and 0.0015 mole of (XIII) was allowed to stand for 2 hours at room temperature and was then heated slightly until the residue completely dissolved. The alcohol was distilled off under vacuum at 30-40°. 5.0 ml of water was added to the residue and the solution was acidified to congo with hydrochloric acid. (XV) was precipitated as an oil which crystallized immediately. The product was filtered by suction, washed with alcohol (2 × 2.0 ml) and recrystallized from a mixture of benzene and petroleum ether (1:1). The yield was 80.3%. (XV) was in the form of colorless prisms with an m. p. of 188-190°; it was readily soluble in alkalis.

Found %: N 5.50. Equiv. 1.03. $C_{27}H_{19}O_6N_2P$. Calculated %: N 5.62. Equiv. 1.00.

B. Saponification of (XIV). This was carried out in the same way; the yield was 53.6%. Samples of (XV), obtained by the saponification of (XIII) and (XIV), and also as a by-product during the preparation of (XII) and (XIV), were identical since a mixed melt showed no depression of the melting point.

SUMMARY

Trichlorophosphazo acyls of diphenylchloracetic, triphenylacetic and p-nitrobenzoic acids were prepared and their thermal stability studied.

It was shown that trichlorophosphazo acyls exist not only for trichloroacetic acid and its analogs but also for diphenylchloroacetic and p-nitrobenzoic acids. Because of the insufficient thermal stability of the diacyl chloride of triphenylacetylamidophosphoric acid it was not possible to obtain trichlorophosphazotriphenyl acetyl.

The corresponding di- and tri-α-naphthoxy derivatives were obtained from the synthesized trichlorophosphazo- and trichloroisophosphazo compounds and their properties were studied.

The first crystalline derivative of trichloroisophosphazo acyls, tri-α-naphthoxyisophosphazo-p-nitrobenzoyl, was obtained.

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THE ABSORPTION SPECTRA AND STRUCTURES OF SUBSTITUTED QUINOLINES, USED AS STARTING MATERIALS FOR ANTI-MALARIALS

IV. ABSORPTION SPECTRA AND STRUCTURE OF NEOPLASMOQUIN

V. I. Bliznyukov and L. S. Sokol

The absorption spectra of 8-(5'-diethylamino-2'-pentyl)-aminoquinoline (neoplasmoquin), that we investigated, were found to be complex and in order to interpret them, we studied the absorption spectra of 8-aminoquinoline.

EXPERIMENTAL

The neoplasmoquin was synthesized according to the data in [1]. Before examination, the materials were purified by vacuum distillation and 8-aminoquinoline was futher purified by a second recrystallization from heptane.

In the spectrographic examinations we used solutions in anhydrous hexane, hexane containing 0.04–0.07% of water, tetrachloromethane, dioxan , ethanol, glycol and water. The solution concentrations used were from $2 \cdot 10^{-2}$ to $2 \cdot 10^{-5}$ M.

According to the data of Steck and Ewing [2], 8-aminoquinoline in ethanol has two absorption bands. We also found two absorption bands for it in a hexane solution. In the general appearance and the position of the bands, the spectrum of 8-aminoquinoline is similar to the spectra of ortho-derivatives of benzene, containing one electron-attracting and one electron-donating substituent in the ring. For example, there is a similarity to the spectral curves of o-nitroaniline or o-hydroxyacetophenone (Fig. 1, curves 1 and 4). According to this, these bands of 8-aminoquinoline should be ascribed to the benzene bands, known briefly as "ortho-type" bands (Table 1).

TABLE 1

Compounds (dissolved in hexane)	Long wavelength ortho-type benzene band		Pyridine band		Short wavelength ortho-type benzene band	
	λ	ε	λ	ε	λ	ε
8-Aminoquinoline	3440	4000	—	—	2520	40000
2-Aminoquinoline	3330	6000	2730 *	4000	2340	50000
2-Hydroxyacetophenone [12]	3250	3500	—	—	2510	9000
Pyridine, spectrum displaced toward longer wavelengths by 250 A	—	—	2800	2000	—	—

It should be noted that the main spectrum of 4-aminoquinoline in hexane is a "benzene – pyridine" spectrum, characterized by two "benzene" and one "pyridine" absorption band [3], and not a spectrum of the "para-type" as might have been expected in analogy with the spectrum of 8-aminoquinoline. The absence of a pyridine band in the spectrum of a hexane solution of 8-aminoquinoline may be due to intramolecular association and we therefore continued the investigation using tetrachloromethane as solvent as this eliminates molecular association. In fact, the spectrum of a tetrachloromethane solution of 8-aminoquinoline showed a pyridine absorption band (Fig. 1, curve 3), which was inserted into the main "ortho-benzene" spectrum and shifted the minimum, dividing the two ortho-type bands from each other. Due to this, the long wavelength band of 8-aminoquinoline seemed to narrow, while the pyridine band maximum was cut off, especially at the short wavelength side, by the more intense, short wavelength, ortho-type band.

The absorption spectrum of neoplasmoquin in tetrachloromethane was likewise characterized by two ortho-type bands, on which a third band, the pyridine one, with an indefinite absorption maximum, was superimposed. In comparison with the band of pyridine itself, this pyridine band of quinoline derivatives was displaced bathochromically by approximately 200-250 A under the effect of the substituent benzene ring. The same was observed for 2-aminoquinoline (Fig. 2, curves 1, 3, 4, 5).

TABLE 2

Compounds (dissolved in tetrachloromethane)	Long wavelength ortho-type benzene band		Pyridine band		Short wavelength ortho-type benzene band	
	λ	ε	λ	ε	λ	ε
Neoplasmoquin	3720	6000	2800 •	6000	2540 •	50000
8-Aminoquinoline	3420	8000	2800 •	6000	2540 •	50000

On the basis of this similarity, the spectra of neoplasmoquin and 8-aminoquinoline in tetrachloromethane may be considered as complex ortho-benzene and pyridine absorption spectra.

By comparing the absorption spectrum curves of neoplasmoquin and 8-aminoquinoline in tetrachloromethane, it was established that the effect of the diethylaminopentyl radical appeared only as a displacement of the neoplasmoquin long wavelength band toward the visible spectrum by approximately 300 A, while the pyridine band was not displaced. The absorption band maxima are compared in Table 2.

Under the effect of dipolar solvents, the complex ortho-benzene and pyridine spectra of neoplasmoquin and 8-aminoquinoline changed mainly in the region of the pyridine absorption spectra. Thus, for example, no pyridine absorption band was detected on the absorption spectrum curves of neoplasmoquin dissolved in dioxan or ethanol (Fig. 2, curves 2 and 1; compare with Fig. 1, curves 2 and 3). Due to the decrease in the intensity of the pyridine absorption band, the minimum dividing the two ortho-benzene bands of neoplasmoquin deepened almost four-fold. At the same time the long wavelength ortho-benzene band widened and a new band appeared in the form of a bend with a maximum at approximately λ 3230 A and ε 2000. Approximately the same changes were observed in the spectrum of 8-aminoquinoline, dissolved in ethanol or hexane, containing 0.04% water, as in the spectrum of neoplasmoquin affected by ethanol or dioxan.

In going from ethanol to glycol, the new absorption band of 8-aminoquinoline with a maximum at λ 3230 A was seen more clearly on the spectrum curve (Fig. 3, curves 2 and 4). Here, the intensity of both ortho-type 8-aminoquinoline bands increased while the depth of the minimum, dividing the two ortho-type bands, decreased even more than in ethanol.

It was noted that by introducing an electron donor substituent (NH_2, OH) into position 8 of 8-aminoquinoline, its ortho-benzene bands were displaced bathochromically without essentially changing the pyridine absorption spectrum. Using this factor, we were able to separate the ortho-benzene bands and, using 6-hydroxy-8-(3'-diethylamino-1'-propyl)-aminoquinoline (quinoline-54) as an example, showed that the bend in the curve with a maximum approximately at λ 3230 A, which appeared in the spectra of neoplasmoquin or 8-aminoquinoline under the effect of dipolar solvents, did in fact correspond to the new absorption band (Fig. 3, curves 1, 5). By its origin, the band with the λ 3230 A maximum should be assigned to the band of ortho-substituted

benzene with two electron donor substituents. However, such a band, for example in o-phenylenediamine, has a maximum at λ 2920 A, while the maximum of the corresponding band of 8-aminoquinoline is displaced by more than 250 A into the visible region. We shall conditionally call this band the "o-phenylenediamine" band of neoplasmoquin or 8-aminoquinoline. The measurement data are given in Fig. 3 and the absorption band maxima are compared in Table 3.

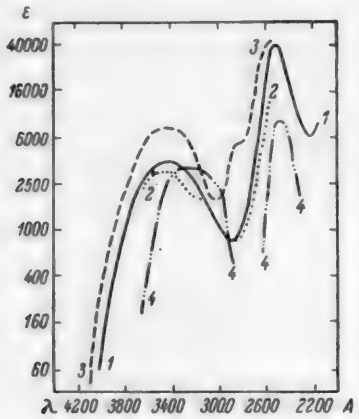


Fig. 1. Absorption spectra. 1) 8-Aminoquinoline in hexane, 2) 8-aminoquinoline in hexane, containing 0.04% water, 3) 8-aminoquinoline in tetrachloromethane, 4) 2-hydroxyacetophenone in hexane, according to data [12].

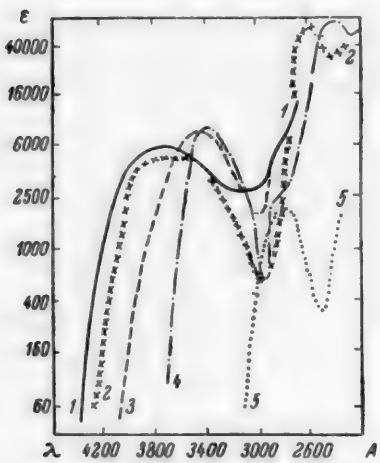


Fig. 2. Absorption spectra. 1) Neoplasmoquin in tetrachloromethane, 2) neoplasmoquin in dioxan, 3) 8-aminoquinoline in tetrachloromethane, 4) 2-aminoquinoline in ethanol, 5) pyridine in hexane (the spectrum was displaced 250 A toward longer wavelengths).

A comparison of the absorption curves of 8-aminoquinoline in water and in hexane (Fig. 3, curve 3 and Fig. 1, curve 1; compare Fig. 1, curves 1 and 2) showed that under the effect of water the maximum of both ortho-type bands was displaced toward shorter wavelengths. At the same time, the maximum of the band, similar to that of o-phenylenediamine, was displaced toward shorter wavelengths.

DISCUSSION OF RESULTS

On the basis of the experimental data given above, the absorption spectra of neoplasmoquin and 8-aminoquinoline in tetrachloromethane were considered as complex ortho-benzene and pyridine absorption spectra. Under the effect of dipolar solvents (water, ethanol) this complex spectrum changed mainly in the region of the pyridine absorption spectrum. In this case, a band was superimposed on the ortho-benzene spectrum, as found in ortho-derivatives of benzene with two electron donor substituents, and this band was named conditionally the o-phenylenediamine band and had a maximum at approximately λ 3230 A. The changes in neoplasmoquin and 8-aminoquinoline spectra in ethanol, glycol or wet hexane may be explained by bonding of the "unshared" electron pair of the ring nitrogen by the solvent molecules. The appearance of the o-phenylenediamine band in the spectra but with the retention of the ortho-benzene absorption spectrum, under the effect of these solvents may denote the capacity of the ring nitrogen to donate electrons.

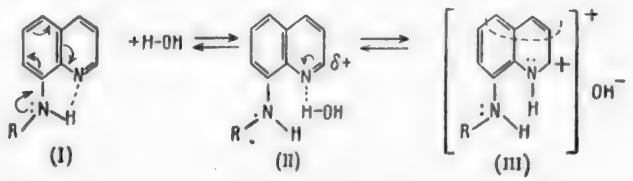
The formation of two ortho-type bands and one pyridine band in the neoplasmoquin spectrum may be explained, using the rules established by N. A. Valyashko [7], by the conjugation of the ring nitrogen (electron attracting) with the π-electrons of the benzene ring and NHR-group in position 8. This conjugation must be maintained by an intramolecular hydrogen bond (I). In dipolar solvents the ring nitrogen of neoplasmoquin adds a solvent molecule (water) with its unshared electron pair when the intramolecular hydrogen bond (II) opens. Then the electron density is so distributed in the pyridine ring that the positive charge on the 2nd carbon atom is partly increased (δ+), and as a result the aromatic character of the pyridine ring partially decreases. The subsubsequent ionization fixes the positive charge on

TABLE 3

Compound	Solvent	Long wavelength ortho-type benzene band		o-Phenylene-diamine band		Short wavelength ortho-type benzene band	
		λ	ε	λ	ε	λ	ε
8-Aminoquinoline	Ethanol	3370	9000	3150 *	2000	2550	32000
	Water	3260	4000	3000 *	3000	2460	32000
	Glycol	3460	7500	3230	6600	2530	36000
Neoplasmoquin	Dioxan	3730	4500	3230 *	2000	2530	50000
6-Hydroxy-8-(3'-diethylamino-1'-propyl)-aminoquinoline (quinoline 54)	1 M sodium ethoxide	3910	3200	3240	2400	2790	36000
o-Phenylenediamine [13]	Ethanol	–	–	2920	1600	–	–

* Taking the middle point at the bend in the curve.

the 2nd carbon atom and in the ion formed (III) the pyridine ring may be considered as having two substituents – the vinyl group and nitrogen of the ring (as a substituted amino group), which become conjugated with the π-electron system of the benzene ring.



The vinyl group forms a conjugated system with two ethylene bonds, shown by the dotted lines in formula (III), and the nitrogen of the ring is conjugated with the π-electrons of the benzene ring and NHR-group, as in o-phenylenediamine.

Thus, the absorption spectra in a tetrachloromethane solution establish that the neoplasmoquin ring nitrogen is capable of attracting electrons from the benzene ring and is conjugated with the NHR-group in position 8. However, under the effect of dipolar solvents, the ring nitrogen may donate electrons to the benzene ring.

The secondary NHR-group and its tendency for forming an intramolecular hydrogen bond are the main factors in making the ring nitrogen of neoplasmoquin capable of attracting and donating electrons. In this, the benzene is of greater importance than the pyridine ring [3]. This is confirmed by the fact that hydrogenation of the quinoline system's pyridine ring does not destroy the anti-malarial activity of plasmoquin [8].

K. S. Topchiev, M. M. Yakshin and R. E. Shindel [9] were the first to measure the dipole moment of neoplasmoquin but they drew no conclusions from the values they obtained. A comparison of the data available shows a considerably smaller dipole moment for neoplasmoquin than for unsubstituted quinoline (Table 4).

The experimental values for the dipole moments of these compounds agree well with those calculated using the differences of the dipole moments of the quinoline ring and the side chain. Such an agreement, according to data in [10], may occur only with a definite molecular configuration and must be due to the side chain being in a position parallel to the vector moment of quinoline. The steric position of the neoplasmoquin side chain in a plane, parallel to the plane of the quinoline ring, apparently, promotes the formation of an intramolecular hydrogen bond with the ring nitrogen using the NHR-group hydrogen. According to D. N. Shigorin's definition [11], by its nature, such a cyclic hydrogen bond should be considered as an intramolecular hydrogen

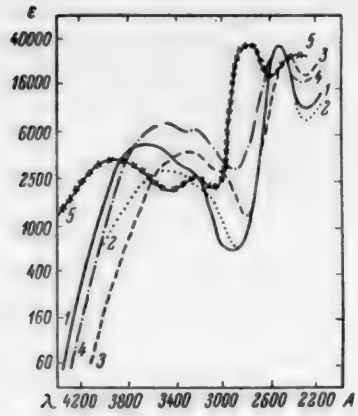
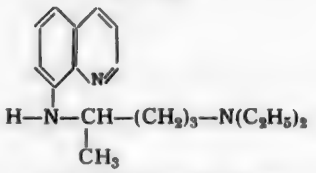


Fig. 3. Absorption spectra. 1) Neoplasmoquin in ethanol, 2) 8-aminoquinoline in ethanol, 3) 8-aminoquinoline in water, 4) 8-aminoquinoline in glycol, 5) 6-hydroxy-8-(3'-diethylamino-1'-propyl)-aminoquinoline (or quinoline-54) in a 1 M sodium ethoxide solution.

bond with π-electron interaction. Transfer of the π-electron interaction in a neoplasmoquin molecule is possible with a planar disposition of the side chain when the π-electrons of all the molecule, i.e., the benzene and pyridine rings of the neoplasmoquin, may enter the reaction, as we previously showed schematically (I).

An indirect proof of the formation of an intramolecular hydrogen bond with π-electron interaction in neoplasmoquin is the displacement toward longer wavelengths of the neoplasmoquin o-phenylenediamine band in comparison with the corresponding o-phenylenediamine band. This difference is due to the formation of unequivalent intramolecular hydrogen bonds in 8-aminoquinoline and in o-phenylenediamine [14]. Spectrographic investigation in the infrared region did, in fact, prove the presence of an intramolecular hydrogen bond in 8-aminoquinoline [4]. A similiar ortho-effect was also indicated by measurements of the basicity of 8-aminoquinoline [5]. Its basicity is less than that of quinoline and is similar to the basicity of α-naphthylamine. Data on the relative pK_{acid} values of quinoline acids and hydrolysis rates of their esters [6] also confirm the hypothesis of the existence of a hydrogen bond.

TABLE 4

Compound	Formula	Value of dipole moment (in D)
Quinoline		2.18 [9]
Neoplasmoquin		0.70 [9]
1-Diethylamino-4-amino-pentane	$H_3C-CH(CH_2)_3N(C_2H_5)_2$ NH_2	1.36 [10]

SUMMARY

1. We studied the effect of solvents on the absorption spectra of 8-(5'-diethylamino-2'-pentyl)-aminoquinoline (neoplasmoquin) and 8-aminoquinoline.

2. We established the similarity between the spectrum of neoplasmoquin in a tetrachloromethane solution and the spectra of 8-aminoquinoline and those ortho-derivatives of benzene that have one electron-donor and one electron-acceptor substituent; furthermore, a band found in the pyridine spectrum is superimposed on this "ortho-type" of spectrum.

3. Under the effect of hexane and dipolar solvents, the "pyridine" band disappears in the neoplasmoquin spectrum while a band is superimposed onto the "ortho-benzene" spectrum, such as occurs in ortho-benzene derivatives with two electron-donor substituents.

4. It was established that, in tetrachloromethane solution, the nitrogen of the neoplasmoquin ring is capable of attracting electrons from the benzene ring and entering conjugation with the NHR-group in position 8, but under the effect of dipolar solvents, which bind its unshared electron pair, it can donate electrons to the benzene ring.

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REACTION OF α-ALKOXYACRYLONITRILES WITH MERCURIC ACETATE

PREPARATION OF ESTERS OF MONOMERCURATED ACETIC ACID

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Ketene acetals, which have a highly active double bond, do not react with mercuric acetate to give esters of monomercurated acetic acid [1]. With the aim of preparing such esters, we decided to investigate the reaction of mercuric acetate with α-alkoxyacrylonitriles $CH_2=C(OR)CN$. α-Alkoxyacrylonitriles, which may be considered as ketene acetals, with one alkoxy group substituted by a nitrile group, have a double bond that is noticeably more passive than those of ketene acetals or even of vinyl ethers. Whereas vinyl butyl ether reacts with mercuric acetate vigorously in a fraction of a minute with the evolution of heat, the reaction with α-butoxyacrylonitrile requires several hours. The study of mercuric acetate addition to α-alkoxyacrylonitrile is also interesting as it includes a case of competing orientations of addition and little attention has been paid to this phenomenon in the aliphatic series. On the basis of what we know on competing orientations in the aromatic series, we would expect that the alkoxy group would determine the direction of addition and that a mercury atom would thus add to the CH_2 group of α-alkoxyacrylonitrile. The organomercury derivative formed as an intermediate, which has three different substituents at one carbon atom, then decomposes in an interesting way to give an ester of monomercurated acetic acid:

$$CH_2=C(OR)(CN) + (CH_3COO)_2Hg + H_2O \longrightarrow \left[CH_3COOHgCH_2C(OR)(CN)(OH)\right] \xrightarrow{Hg(CH\,COO)_2}$$

$$\longrightarrow CH_3COOHgCH_2COOR + Hg(CN)_2 + 2CH_3COOH$$

This direction of the reaction is promoted by the following factors: 1) the strong displacement of the electrons under the effect of the mercury atom and alkoxyl group toward the electron-acceptor nitrile group; 2) removal of this group as the anion CN^- by mercuric acetate to form mercuric cyanide, which is weakly dissociated.* 2 moles of the mercury salt must be used for the formation of one mole of monomercurated acetic ester as one mole of mercury salt is converted into mercuric cyanide, which is incapable of addition at a multiple bond. Actually, if 1 mole of mercuric acetate is taken per mole of α-butoxyacrylonitrile then the yield of the butyl ester of mercurated acetic acid is only 43%. On reacting α-alkoxyacrylonitriles with twice the amount of mercuric acetate the yield of mercurated acetic esters was 90-95%.

We synthesized methyl, ethyl, propyl and butyl esters of acetatomercuriacetic acid by the reaction described. These compounds were crystalline materials with a definite melting point and crystallized well from methyl and ethyl alcohol. The lower samples of this series were readily soluble in water. Exchange reactions with potassium halides gave ethyl, propyl and butyl esters of chloromercuri- and bromomercuriacetic acid, which were compounds that readily crystallized from diethyl ether.

It is known that mercuric salts are added to unsaturated compounds more readily in an alcoholic rather than in an aqueous medium; however, this reaction could not be carried out in the case of α-alkoxyacrylonitriles.

* Apparently, mercuric acetate may be used successfully instead of silver oxide for the cyanohydrin decomposition, as the formation of the weakly dissociated mercuric cyanide would displace the equilibrium toward the formation of the carbonyl compound.

The homologs of α-alkoxyacrylonitriles, $CH_3CH=C(OC_2H_5)CN$ and $C_2H_5CH=C(OC_2H_5)CN$, also did not react with mercuric acetate.

The starting methoxy- and ethoxyacrylonitriles were prepared by Guvigny and Normant's method [2]. We were the first to obtain propoxy- and butoxy-acrylonitriles using a similiar method.

EXPERIMENTAL

Preparation of α-propoxy-β-bromopropionitrile. 373.5 g (1.5 moles) of α,β-dibromoethyl propyl ether was quickly added with cooling and stirring to a suspension of 135.7 (1.5 moles) of cuprous cyanide in 375 ml of absolute ether and the mixture stirred for 1 hour at room temperature and for 2 hours while heated on a water bath. After cooling, the mixture was centrifuged, the solvent distilled off and the residue vacuum distilled to give a fraction 86-88° (7.5 mm). The yield was 162.3 g (55.8%).

α-Butoxy-β-bromopropionitrile (b. p. 90-100° at 8 mm) was prepared in 38% yield similarly.

These compounds rapidly decomposed on distillation and storage and they were therefore quickly used for subsequent reactions.

Preparation of α-propoxyacrylonitrile. With constant stirring, 81.5 g (0.8 mole) of diethylamine was added dropwise to a mixture of 162 g (0.8 mole) of α-propoxy-β-bromopropionitrile and an equal volume of absolute ether. The precipitate of amine salt formed was separated off from the liquid and washed twice with ether. The ether was distilled off and the residue vacuum distilled. We collected a fraction 55-61° (20 mm). In a second distillation, we collected a substance with b. p. 59.5° (20 mm). The yield was 68.5 g (73%).

n_D^{20} 1.42305, d_4^{20} 0.8996, MR_D 31.46; calc. 30.9.
Found %: C 64.66, 64.53; H 8.16, 8.32. C_6H_9ON. Calculated %: C 64.83; H 8.16.

α-Butoxyacrylonitrile was prepared similarly. In the first distillation we collected a fraction 59-64° (10 mm) and in the second, one boiling at 63.2° (10 mm). The yield was 65%.

n_D^{20} 1.4279, d_4^{20} 0.8924, MR_D 36.07; calc. 35.52.
Found %: C 66.95, 67.06; H 8.90, 8.92. $C_7H_{11}ON$. Calculated %: C 67.16; H 8.85.

Reaction of α-propoxyacrylonitrile with mercuric acetate. 63.6 g (0.2 mole) of mercuric acetate was dissolved in 150 ml of hot water and 11.1 g (0.1 mole) of α-propoxyacrylonitrile was added to the cooled solution in several portions with vigorous shaking. A white precipitate, which quickly formed, was separated off. The mother liquors were evaporated down in the cold and the mercury compound, which separated, was again collected. The total yield of the propyl ester of acetatomercuriacetic acid was 34.6 g (95%). The material crystallized from methyl alcohol. The m. p. was 109-111°.

Found %: C 23.56, 23.11; H 3.53, 3.45; Hg 55.71, 55.82. $C_7H_{12}O_4Hg$. Calculated %: C 23.30; H 3.35; Hg 55.61.

Reaction of the propyl ester of acetatomercuriacetic acid with potassium chloride. 3.6 g (0.01 mole) of the propyl ester of acetatomercuriacetic acid was dissolved in 30 ml of hot water. 0.75 g (0.01 mole) of potassium chloride, dissolved in 6 ml of hot water, was poured into the hot solution obtained in portions. An oil precipitated. The oil was separated from the aqueous part. The aqueous part was extracted with ether, the ether extracts combined with the oil and the ether evaporated off. There remained the crystalline propyl ester of chloromercuriacetic acid with m. p. 59-62°.

Found %: Hg 59.78, 59.76. $C_5H_9O_2ClHg$. Calculated %: Hg 59.51.

Reaction of the propyl ester of acetatomercuriacetic acid with potassium bromide. 3.6 g (0.01 mole) of the propyl ester of acetatomercuriacetic acid was dissolved in 30 ml of hot water and to the solution obtained was added a solution of 1.2 g (0.01 mole) of potassium bromide in four portions. An oil precipitated. The solution was cooled, the oil separated and the aqueous part extracted with ether. The ether extracts were

Synthesized Esters of Mercurated Acetic Acid

Formulas of the substances	Yield (in %)	Melting point	Found (in %)			Calculated (in %)		
			C	H	Hg	C	H	Hg
$CH_3COOHgCH_2COOCH_3$	—	135—136°	17.81, 18.07	2.45, 2.51	60.40, 60.71	18.04	2.42	60.26
$CH_3COOHgCH_2COOC_2H_5$	89	116	20.38	3.03	58.06, 58.35	20.78	2.90	57.85
$ClHgCH_2COOC_2H_5$	92	66	—	—	61.89, 61.87	—	—	62.07
$BrHgCH_2COOC_2H_5$	54	43—45	—	—	54.64, 54.68	—	—	54.56
$CH_3COOHgCH_2COOC_3H_7$	95	109—111	23.56, 23.11	3.53, 3.45	55.71, 55.82	23.30	3.35	55.61
$ClHgCH_2COOC_3H_7$	82	59—62	—	—	59.78, 59.76	—	—	59.51
$BrHgCH_2COOC_3H_7$	73	42—43	—	—	53.05, 52.84	—	—	52.56
$CH_3COOHgCH_2COOC_4H_9$	90	89—91	25.70, 25.75	3.89, 3.84	53.81, 53.90	25.63	3.76	53.52
$BrHgCH_2COOC_4H_9$	75	30	—	—	50.63, 50.42	—	—	50.70

combined with the oil; after evaporation of the ether, there was left the crystalline propyl ester of bromomercuriacetic acid with m. p. 42-43°

Found %: Hg 53.05, 52.84. $C_5H_9O_2BrHg$. Calculated %: Hg 52.56.

The other esters of mercurated acetic acid were prepared by similar methods (see Table).

SUMMARY

1. It was established that α-alkoxyacrylonitriles reacted with mercuric acetate in an aqueous medium to give esters of monomercurated acetic acid esters in high yield.

2. A mechanism was put forward for the reaction of α-alkoxyacrylonitriles with mercuric acetate in an aqueous medium.

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TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

X. THE RELATIVE EFFECT OF CATALYSTS IN THE ACYLATION OF BENZENE AND THIOPHENE WITH TETRAACYLOXYSILANES

Yu. K. Yuryev, Z. V. Belyakova and N. S. Zefirov

In previous papers we showed that acylation of heterocyclic compounds of an aromatic nature (thiophene, pyrrole, selenophene), with mixed anhydrides of orthosilicic acid and organic acids (monobasic and dibasic acid and monoethyl esters of dibasic acids) gave high yields of the corresponding ketones [1-4] and ketoacids [5, 6]. Acylation of thiophene and selenophene with silicoanhydrides of saturated monobasic acids to form ketones, proceeded in the presence of anhydrous stannic chloride in a benzene medium; acylation of thiophene with silicoanhydrides of saturated dibasic acids to give ketoacids, proceeded in the presence of anhydrous aluminum chloride in a nitrobenzene medium; acylation of selenophene with silicoanhydrides of monoethyl esters of dibasic acids to give ketoacids, proceeded in a benzene medium in the presence of anhydrous stannic chloride.

It is known from the literature data that, besides anhydrous aluminum chloride and stannic chloride, the Gustavson-Friedel-Krafts reaction is also catalyzed by anhydrous beryllium chloride [7], zinc chloride [8-10], titanium tetrachloride [11], zirconium tetrachloride, [12], antimony pentachloride [13], boron fluoride [14, 15], ferric chloride [16] etc. Dremer, et al., [13, 17] investigated the activity of a large number of catalysts using the synthesis of p-methylacetophenone as the example and Harthough and Kosak [18-24] did likewise using the synthesis of acetothienone.

The aim of this work was to study the relative effect of a series of catalysts on the acylation of thiophene and benzene with tetraacetoxysilane and the mixed anhydride of orthosilicic acid and acetic acid. Silicoacetic anhydride was chosen as a standard as it is readily prepared in a pure form by reacting silicon tetrachloride with acetic anhydride [25] and is formed even more readily by the reaction of silicon tetrachloride with acetic acid in an inert solvent, in which it is used for further reactions without additional purification [1]. In our papers on the acylation of compounds of an aromatic nature mentioned above, the acylating agents we used were silicoanhydrides, prepared in a solvent and not isolated from it in a pure state.

In this work we studied the reactivity of both samples of silicoacetic anhydride in order to find out whether thiophene, selenophene and benzene are actually acylated by silicoanhydrides of the organic acids themselves or whether there is the participation of acid chlorides, which could be formed by the action of silicon tetrachloride on the previously formed silicoanhydride during its preparation in an inert solvent:

$$4RCOOH + SiCl_4 \longrightarrow Si(OCOR)_4 + 4HCl$$
$$Si(OCOR)_4 + SiCl_4 \longrightarrow 4RCOCl + 2SiO_2$$

Due to the method used for isolating it, the silicoacetic anhydride prepared by reacting silicon tetrachloride with acetic anhydride, should not contain acetyl chloride and we therefore call it "pure silicoacetic anhydride."

The experiments on the acylation of benzene and thiophene with the two samples of silicoacetic anhydride were carried out under the same conditions in the presence of anhydrous aluminum and ferric chlorides, and stannic and zinc chlorides, respectively. The results obtained in these experiments are given in Table 1.

TABLE 1

Catalyst	Material being acylated	Acylating agent – silicoacetic anhydride	Yield of ketone (in %)
Aluminum chloride	Benzene	Pure	47.0
		Prepared in solvent	47.0
Ferric chloride	Benzene	Pure	40.0
		Prepared in solvent	40.0
Stannic chloride	Thiophene	Pure	94.3
		Prepared in solvent	94.0[1]
Zinc chloride	Thiophene	Pure	46.5
		Prepared in solvent	46.0

The data in Table 1 show that the yield of each ketone did not depend on which sample of silicoacetic anhydride was used in preparing it and this indicated that the silicoanhydride was actually the acylating agent in the reaction described. If in preparing silicoacetic anhydride in a solvent, an acid chloride (acetyl chloride) was formed, then probably only a very small amount was produced. If the opposite were the case, then the ketone yields, in acylation with "pure silicoacetic anhydride," would be noticeably less as acetyl chloride is one of the most vigorous acylating agents.

As we had established that the ketone yield did not depend on which of the two samples of silicoacetic anhydride was used for the acylation of benzene and thiophene, we used pure silicoacetic anhydride for further study of the activity of catalysts, as it can be readily stored; anhydrous beryllium chloride, titanium tetrachloride and boron fluoride and its etherate were used in the acylation of benzene and thiophene. The results obtained in this series of experiments are given in Table 2.

TABLE 2

Acylating agent	Material being acylated	Catalyst	Molar ratio of catalyst : acetic acid	Maximum reaction temperature	Ketone yield (in %)
Silicoacetic anhydride, prepared in a solvent	Benzene	$FeCl_3$	2 : 1	100°	36.0
			1 : 1	100	40.0
			0.5 : 1	—	—
Pure silicoacetic anhydride	Thiophene	$TiCl_4$	0.4 : 1	100	14
			0.4 : 1	20	0.0
			0.4 : 1	40	24.5
			0.4 : 1	60	37.0
			0.83 : 1	60	93.5
Pure silicoacetic anhydride	Thiophene	$ZnCl_2$	2 : 1	100	46.5
			1 : 1	100	18.0
Pure silicoacetic anhydride	Thiophene	$BeCl_2$	2 : 1	100	36.0
			1 : 1	100	31.5
Pure silicoacetic anhydride	Thiophene	$BF_3 \cdot O(C_2H_5)_2$	0.1 : 1	100	0.0
			0.5 : 1	100	0.0
			1 : 1	100	25.5
			2 : 1	100	24.5
Pure silicoacetic anhydride	Thiophene	BF_3	—	0	32.0
			—	25	45.0
			—	60	45.0

The data in Table 2 show that the acylation of thiophene in the presence of titanium tetrachloride proceeded with as high a yield as in the presence of stannic chloride and may be of preparatory value. The acylation product yield depended not only on the temperature at which the reaction occurred but also on the catalyst-acylating agent ratio. In connection with this, the following specific property of the reaction studied

should be noted: in the acylation of thiophene with anhydrides of organic acids, a catalytic amount of the catalyst is required [19, 20, 23, 24], while in acylation with silicoanhydrides of organic acids, molar or even larger amounts of catalyst are required; the ratio catalyst : silicoacetic anhydride was 0.5:1, 1:1, 2:1 (calculated on the acetic acid).

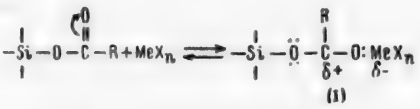
Experiments on the acylation of benzene in the presence of anhydrous titanium tetrachloride, zinc chloride, beryllium chloride and boron fluoride and its etherate gave negative results. This showed that activity in acylation decreased in the order: acid chloride > anhydride > silicoanhydride.

Negative results were also obtained in experiments on the acylation of thiophene with silicoacetic anhydride in the presence of anhydrous aluminum chloride in a benzene medium (adapted to Peter's method [26]) and in a cyclohexane medium and in the presence of 85% phosphoric acid: in the presence of aluminum chloride, resinification and destruction of thiophene with the evolution of hydrogen sulfide occurred; on adding phosphoric acid a white, viscous mass precipitated and no acetothienone was formed.

The analogy between the chemical behavior of silicoanhydrides and the anhydrides of organic acids, which was pointed out by Yu. K. Yuryev and G. V. Elyakov [27], was confirmed convincingly by the acylation of thiophene in the presence of boron fluoride and its etherate.

The mechanism of thiophene acylation with tetraacyloxysilanes may be represented by the following scheme.

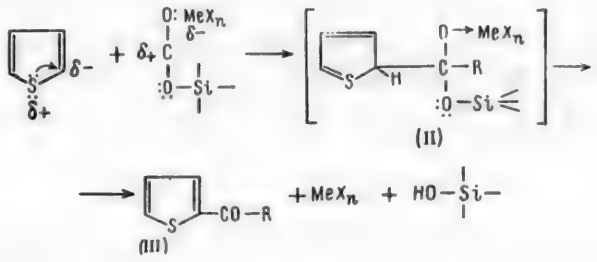
1. An active complex of tetraacyloxysilane with the catalyst (I) is formed



(I)

Me=Be, Zn, B, Al, Fe, Ti, Sn .

2. The active complex reacts with a thiophene molecule to form an addition product (II) or ternary complex which is further decomposed to form the ketone (III) and silicic acid.



(II)

(III)

As regards the evolution of hydrogen halide during the acylation of thiophene and benzene with tetraacyloxysilanes, it is probably due to the silicic acid formed reacting with the catalyst by the reaction

$$Si(OH)_4 + 4MeX_n \rightarrow 4HX + Si(OMeX_{n-1})_4$$

We established in this work that when boron fluoride and its etherate were used, a similiar reaction occurred according to the equation

$$3Si(OH)_4 + 4BF_3 \rightarrow 4H_3BO_3 + 3SiF_4$$

EXPERIMENTAL

Experimental procedure. In a three-necked, round-bottomed flask (500 ml) fitted with a reflux condenser with a calcium chloride tube and a stirrer, silicoacetic anhydride was prepared from 5.1 g (0.03 mole) of silicon tetrachloride and 6 g (0.1 mole) of glacial acetic acid in 125 ml of anhydrous benzene, as we described previously [1], or 6.6 g (0.25 mole) of pure silicoacetic anhydride, prepared by treating silicon tetrachloride with acetic anhydride [25], was dissolved in 125 ml of anhydrous benzene. The silicoacetic anhydride obtained by the given method was (in addition to the usual procedure) washed 3 times with absolute ether.

The liquid catalysts were dissolved in 30 ml of dry benzene and added dropwise in the cold with continuous stirring to the benzene solution of the silicoanhydride, to which 7 g (0.083 mole) of thiophene had previously been added in the case of the acetothienone preparation. The solid, well powdered catalysts were added in the cold in small portions with constant stirring. Boron fluoride was introduced into the reaction mixture via a tube leading to the bottom of the flask.

After the introduction of the catalyst, the reaction mixture was heated on a water bath with a slow increase in temperature until the evolution of hydrogen chloride ceased, or, in the case of boron fluoride etherate, until the evolution of silicon tetrafluoride ceased. Boron fluoride was passed in until saturation was reached, the reaction mixture stirred for a further half hour and the ketone isolated. The acetophenone and acetothienone were isolated as described previously.

Acylation of Benzene

Catalyst – anhydrous aluminum chloride. a) We used 13.2 g of pure silicoacetic anhydride, 30.7 g of aluminum chloride and 125 ml of benzene. We obtained 11.3 g (47.0%) of acetophenone with b. p. 71-72° (8 mm), m. p. 20°.

b) We used 12 g of glacial acetic acid, 10.2 g of silicon tetrachloride, 30.7 g of aluminum chloride and 175 ml of benzene. We obtained 11.3 g (47.0%) of acetophenone with b. p. 75-77° (9 mm), m. p. 19.5°.

Literature data: m. p. 20° [28], m. p. 20.5° [29].

Catalyst – anhydrous ferric chloride. a) We used 6.6 g of pure silicoacetic anhydride, 16.3 g of ferric chloride and 125 ml of benzene. We obtained 4.8 g (40%) of acetophenone with b. p. 68-70° (7 mm), m. p. 20°.

b) We used 6 g of glacial acetic acid, 5.1 g of silicon tetrachloride, 32.5 g of ferric chloride and 125 ml of benzene. We obtained 4.35 g (36%) of acetophenone with b. p. 75-77° (9 mm), m. p. 20°.

c) We used 6 g of glacial acetic acid, 5.1 g of silicon tetrachloride, 16.3 g of ferric chloride and 125 ml of benzene. We obtained 4.8 g (40%) of acetophenone with b. p. 75-77° (9 mm), m. p. 20°.

d) We used 6 g of glacial acetic acid, 5.1 g of silicon tetrachloride and 8.1 g of ferric chloride in 125 ml of benzene. We obtained 2.8 g (23.3%) of acetophenone with b. p. 74-77° (9 mm), m. p. 19°.

Acylation of Thiophene

Catalyst – anhydrous stannic chloride. We used 6.6 g of pure silicoacetic anhydride, 7 g of thiophene, 12 g of stannic chloride and 155 ml of benzene. We obtained 9.9 g (94.3%) of acetothienone:

b. p. 93-95° (12 mm), n_D^{20} 1.5664; d_4^{20} 1.1701, MR_D 35.20. $C_6H_6OSF_2$. Calculated 34.76.

The semicarbazone melted at 186° and a mixed melting point with authentic acetothienone semicarbazone was not depressed.

Literature data for acetothienone: n_D^{20} 1.5662; d_4^{20} 1.167 [30]. b. p. 213.9°, n_D^{20} 1.5667, d_4^{20} 1.1709 [31], b. p. 89.5° (11 mm), n_D^{20} 1.5675; d_4^{20} 1.1750 [1]; for the semicarbazone: m. p. 190° [32], m. p. 186-187° [33].

Catalyst – anhydrous titanium tetrachloride. The acylation experiments were carried out with 6.6 g of pure silicoacetic anhydride, 7 g of thiophene and 7.6 g of titanium tetrachloride in 155 ml of benzene with the reaction mixture at various temperatures (thermometer in the bath):

a) 20°, nc acetothienone was obtained.

b) 40°, we obtained 2.6 g (24.5%) of acetothienone with b. p. 94-96° (13 mm), n_D^{20} 1.5663.

c) 60°, we obtained 3.9 g (37%) of acetothienone with b. p. 90-92° (11 mm), n_D^{20} 1.5664.

d) 100°, we obtained 1.5 g (14%) of acetothienone with b. p. 91-92° (12 mm), n_D^{20} 1.5667.

e) In the experiment we used 6.6 g of pure silicoacetic anhydride, 7 g of thiophene, 16 g of titanium tetrachloride and 155 ml of benzene at 60°. We obtained 9.8 g (93.5%) of acetothienone with b. p. 94-96° (13 mm) n_D^{20} 1.5664, d_4^{20} 1.1720. The semicarbazone melted at 186° and a mixed melting point with authentic acetothienone semicarbazone was not depressed.

Catalyst – anhydrous zinc chloride. a) We used 6.6 g of pure silicoacetic anhydride, 7 g of thiophene, 13.6 g of zinc chloride and 125 ml of benzene. We obtained 1.9 g (18%) of acetothienone with b. p. 94-96° (13 mm), n_D^{20} 1.5663.

b) We used 6.6 g of pure silicoacetic anhydride, 7 g of thiophene, 27.5 g of zinc chloride in 125 ml of benzene. We obtained 4.9 g (46.5%) of acetothienone with b. p. 91-93° (12 mm), n_D^{20} 1.5669, d_4^{20} 1.1720. The semicarbazone melted at 186° and a mixed melting point with authentic acetothienone semicarbazone was not depressed.

c) We used 6 g of glacial acetic acid, 5.1 g of zinc chloride and 125 ml of benzene. We obtained 4.85 g (46%) of acetothienone with b. p. 85-87° (9 mm), n_D^{20} 1.5664, d_4^{20} 1.1703. The semicarbazone melted at 185° and a mixed melting point with authentic acetothienone semicarbazone was not depressed.

Catalyst – anhydrous beryllium chloride. a) We used 6.6 g of pure silicoacetic anhydride, 7 g of thiophene, 8 g of beryllium chloride and 125 ml of benzene. We obtained 3.3 g (31.4%) of acetothienone with b. p. 91-93° (12 mm), n_D^{20} 1.5663, d_4^{20} 1.1701. The semicarbazone melted at 186° and a mixed melting point with authentic acetothienone semicarbazone was not depressed.

b) We used 6.6 g of pure silicoacetic anhydride, 7 g of thiophene, 16 g of beryllium chloride and 125 ml of benzene. We obtained 3.8 g (36%) of acetothienone with b. p. 90-92° (11 mm), n_D^{20} 1.5666, d_4^{20} 1.1710. The semicarbazone melted at 185° and a mixed melting point with authentic acetothienone semicarbazone was not depressed.

Catalyst – boron fluoride etherate. a) We used 6.6 g of pure silicoacetic anhydride, 7 g of thiophene, 28.5 g of boron fluoride etherate and 155 ml of benzene. We obtained 2.6 g (24.5%) of acetothienone with b. p. 90-93° (12 mm), n_D^{20} 1.5670, d_4^{20} 1.1715. The semicarbazone melted at 185° and a mixed melting point with authentic acetothienone semicarbazone was not depressed.

The gas liberated during the reaction was passed into water; a white, amorphous precipitate (silicic acid) and an aqueous solution of fluosilicic acid were formed. Tests for the presence of boric acid both in the precipitate and the solution were negative. From this it follows that the gaseous reaction product was silicon tetrafluoride.

$$3SiF_4 + 4H_2O \rightarrow 2H_2SiF_6 + H_4SiO_4$$

The evolution of silicon tetrafluoride was observed in all experiments in which boron fluoride etherate was used.

It is noteworthy that in contrast to all the experiments with other catalysts, a precipitate of silicic acid was not formed during the decomposition of the reaction complex with water. On evaporating the residue in the flask to dryness after steam distilling off the acetothienone, boric acid was obtained and identified by the preparation of its methyl ester.

b) We used 6.6 g of pure silicoacetic anhydride, 7 g of thiophene, 14.2 g of boron fluoride etherate and 155 ml of benzene. We obtained 2.7 g (25.5%) of acetothienone with b. p. 94-97° (13 mm), n_D^{20} 1.5668, d_4^{20} 1.1711. The semicarbazone melted at 184° and did not depress the melting point of authentic acetothienone semicarbazone.

On introducing 7.1 g and also 1.5 g of boron fluoride etherate into the reaction, no acetothienone was obtained.

Catalyst – boron fluoride. The acylation experiments were carried out with 6.6 g of pure silicoacetic anhydride and 7 g of thiophene in 125 ml of benzene at various temperatures (thermometer in the bath).

a) 0°; we obtained 4.1 g (39%) of acetothienone with b. p. 90-92° (11 mm), n_D^{20} 1.5665, d_4^{20} 1.1710. The semicarbazone melted at 186° and did not depress the melting point of authentic acetothienone semicarbazone.

b) 25°; we obtained 4.7 g (45%) of acetothienone with b. p. 95-97° (13 mm), n_D^{20} 1.5669, d_4^{20} 1.1721. The semicarbazone melted at 185° and did not depress the melting point of authentic acetothienone semicarbazone.

c) 60°; we obtained 4.7 g (45%) of acetothienone with b. p. 95-98° (13 mm), n_D^{20} 1.5666, d_4^{20} 1.1714. The semicarbazone melted at 186° and did not depress the melting point of authentic acetothienone semicarbazone.

As in the previous series of experiments, a precipitate of silicic acid was not formed on decomposing the reaction complex with water; boric acid was found in the residue in the flask after steam distilling off the ketone. This indicates that silicon tetrafluoride was liberated during the introduction of boron fluoride into the reaction.

SUMMARY

1. The acylation of thiophene with silicoacetic anhydride may proceed not only in the presence of anhydrous stannic chloride but in the presence of anhydrous zinc chloride, beryllium chloride and boron fluoride and its etherate as well, with 25.5-46.5% yields, and in the presence of titanium tetrachloride with a 93.5% yield.

2. The acylation of benzene with silicoacetic anhydride occurs both in the presence of anhydrous aluminum chloride and anhydrous ferric chloride. In the presence of anhydrous zinc chloride, beryllium chloride, boron fluoride and its etherate, and titanium tetrachloride, no acylation of benzene with silicoacetic anhydride occurred.

3. The acylation of benzene and thiophene with pure silicoacetic anhydride, prepared from silicon tetrachloride and acetic anhydride and that prepared from silicon tetrachloride and acetic acid in a solvent, gave identical results which indicate conclusively that the silicoanhydride itself is actually the acylating agent.

4. A mechanism scheme for acylation of the thiophene nucleus with silicoanhydrides of organic acids was put forward, based on the analogous chemical behavior of silicoanhydrides and anhydrides of organic acids.

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ETHYLENE SULFIDE IN THE SYNTHESIS OF HETEROCYCLIC COMPOUNDS WITH TWO HETEROATOMS

VI. N-(β-MERCAPTOETHYL)-p-CHLOROANILINE AND ITS CONDENSATION WITH ALDEHYDES, PHOSGENE AND CARBON DISULFIDE

Yu. K. Yuryev, S. V. Dyatlovitskaya and L. G. Bulavin

Ethylene sulfide reacts readily with aniline [1-5] and gives N-(β-mercaptoethyl)-aniline in good yield. The presence of nucleophilic substituents, for example methyl or methoxyl, in the ortho- or para-position of the primary arylamine nucleus does not affect the course of this reaction: the reaction of o- and p-toluidine and o- and p-anisidine with ethylene sulfide also gave the corresponding N-(β-mercaptoethyl)-arylamines in good yields [5]. On the contrary, the presence of electrophilic substituents in the nucleus hinders the reaction with ethylene sulfide and, for example, to prepare N-(β-mercaptoethyl)-o-, m- and p-carbalkoxyanilines from ethylene sulfide and esters of o-, m- and p-aminobenzoic acids more drastic conditions are required, namely long heating of the reagent mixture at 105° in a sealed tube without solvent [6].

In this work we studied the reaction between ethylene sulfide and p-haloanilines. By reacting p-chloroaniline, we prepared N-(β-mercaptoethyl)-p-chloroaniline:

$$H_2C\!\!\diagup\!\!\diagdown CH_2 \;(S) + p\text{-}ClC_6H_4NH_2 \rightarrow p\text{-}ClC_6H_4NHCH_2CH_2SH$$

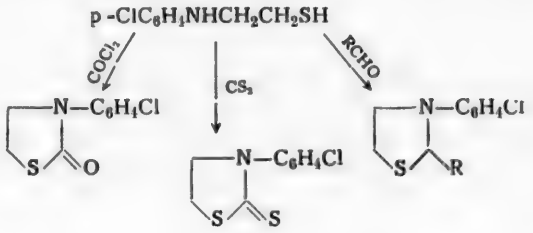
p-Bromo- or p-iodoaniline did not react with ethylene sulfide; in an attempt to isolate N-(β-mercaptoethyl)-p-bromoaniline by distillation of the reaction products, an explosion occurred on reaching 110-115°; when we used p-iodoaniline, a mixture of it with ethylene sulfide in a sealed tube exploded after several minutes heating on a boiling water bath.

Probably, this instability of the N-(β-mercaptoethyl)-p-bromo- and p-iodoaniline formed was due to the lability of the bromine and the even greater lability of the iodine in them, and in connection with this, the possibility of further condensations at the sulfhydryl and amine groups, which would occur on raising the temperature, and the spontaneous evolution of hydrogen halide in these condensations would result in an explosion.

It was noted earlier [2, 6] that aminomercaptans undergo partial decomposition even when distilled in vacuum and due to this, it is difficult to obtain good analytical data for them. We therefore oxidized the N-(β-mercaptoethyl)-p-chloroaniline we prepared with iodine and established that, in contrast to N-(β-mercaptoethyl)-o-, m- and p-carbalkoxyanilines, which form only disulfides in this case, it was converted into the disulfide dihydroiodide as occurred in the case of N-alkylaminoethylmercaptans [2, 7]. The formation of disulfide dihydroiodides or only of disulfides by the oxidation of aminoethylmercaptans with iodine depends, without doubt, on the degree of their basicity and, consequently, on the degree of basicity of the arylamines from which they were prepared [6]. As K_B^{25} for aniline, p-chloroaniline and ethyl p-aminobenzoate are equal to $5.3 \cdot 10^{-10}$, $5.7 \cdot 10^{-10}$ and $2.42 \cdot 10^{-12}$, respectively, the oxidation of N-(β-mercaptoethyl)-p-chloroaniline with iodine naturally resulted in β,β'-di-(p-chlorophenylamino)-diethyl disulfide dihydroiodide.

$$2p\text{-}ClC_6H_4NHCH_2CH_2SH \xrightarrow{I_2} [p\text{-}ClC_6H_4\overset{+}{N}H_2CH_2CH_2S{-}SCH_2CH_2\overset{+}{N}H_2C_6H_4Cl] \cdot 2I^-$$

Similarly to the N-(β-mercaptoethyl)-arylamines we studied previously, N-(β-mercaptoethyl)-p-chloroaniline readily condensed to form a thiazolidine ring: with aldehydes [6, 8] it formed 2-alkyl-(or aryl)-3-p-chlorophenylthiazolidines; with phosgene [9] it gave 3-p-chlorophenylthiazolidone-2; with carbon disulfide [10] it was converted into 3-p-chlorophenylthiazolidinethione-2.



An attempt to metallate 3-p-chlorophenylthiazolidine was unsuccessful: there was no reaction either with magnesium (in diethyl or dibutyl ether) or with lithium (in ether or benzene).

EXPERIMENTAL

N-(β-Mercaptoethyl)-p-chloroaniline. A mixture of 11.7 g (0.195 mole) of ethylene sulfide and 49.8 g (0.390 mole) of p-chloroaniline was heated for 10 hours in a sealed tube on a water bath. On cooling, the reaction mixture partially crystallized; there was excess pressure in the tube. The crystals (unchanged p-chloroaniline) were filtered off and washed with absolute ether; the filtrates were dried with anhydrous magnesium sulfate. The ether was distilled off and the residue vacuum distilled in a stream of nitrogen to give the following fractions: 1st b. p. 110-112° (4 mm), 2.7 g; 2nd b. p. 156-158° (4 mm), 19.7 g; the tarry residue (3.4 g) distilled above 200° with very considerable decomposition.

The 1st fraction quickly crystallized and was unchanged p-chloroaniline; m. p. 71° (from alcohol).

The 2nd fraction was N-(β-mercaptoethyl)-p-chloroaniline, which had the following constants after a second distillation:

b. p. 129-131° (1.5 mm), n_D^{20} 1.6132, d_4^{20} 1.2396, MR_D 52.71. calc. 51.70.

The yield was 19.7 g (54%). On heating the reaction mixture for 5 or 15 hours, the yield was reduced to 34% and 46.5%, respectively.

Found %: C 51.76, 51.63; H 5.53, 5.43; N 7.80, 7.79. $C_8H_{10}NSCl$. Calculated %: C 52.40; H 5.36; N 7.47.

β,β'-Di-(p-chlorophenylamino)-diethyl disulfide dihydroiodide. 0.1 N iodine in alcohol was added dropwise from a burette to 0.4818 g of N-(β-mercaptoethyl)-p-chloroaniline in 3 ml of alcohol until a weak, permanent color appeared and this required 29.85 ml, which corresponds to a 99.2% aminoethylmercaptan content of the sample. The colorless crystals of β,β'-di-(p-chlorophenylamino)-diethyl disulfide dihydroiodide isolated were recrystallized from alcohol; m. p. 176-176.2° (with decomp., in a sealed capillary).

Found %: C 30.91, 30.81; H 3.19, 3.16; N 4.11, 4.24. $C_{16}H_{20}N_2S_2Cl_2I_2$. Calculated %: C 30.54; H 3.20; N 4.45.

A solution of β,β'-di-(p-chlorophenylamino)-diethyl disulfide dihydroiodide in hot, anhydrous alcohol had a reddish color, which disappeared on cooling the solution.

3-p-Chlorophenylthiazolidine. A mixture of 1.88 g (0.01 mole) of N-(β-mercaptoethyl)-p-chloroaniline and 5 ml (0.05 mole) of 30% formalin was shaken for 10 minutes; the mixture gave off heat. The white, crystalline precipitate of 3-p-chlorophenylthiazolidine was filtered off, washed with water until the smell of formaldehyde disappeared, washed with cold alcohol, dried and recrystallized from 80% alcohol; the m. p. was 93-93.5°. The yield was quantitative.

3-p-Chlorophenylthiazolidine was readily soluble in hot, anhydrous alcohol and difficultly soluble in the cold; it was readily soluble in benzene, acetone and dichloroethane, difficultly soluble in ether and insoluble in water.

Found %: C 54.22, 54.10; H 5.08, 5.07; N 6.71, 6.56. $C_9H_{10}NSCl$. Calculated %: C 54.11; H 5.05; N 7.01.

2-Methyl-3-p-chlorophenylthiazolidine. 1.88 g (0.01 mole) of N-(β-mercaptoethyl)-p-chloroaniline in 10 ml of anhydrous alcohol was mixed with 4.4 g (0.1 mole) of acetaldehyde; the mixture gave off heat strongly. The solution was cooled and then 0.3 g of soda crystals in 2 ml of water was added with vigorous stirring. The white crystalline precipitate of 2-methyl-3-p-chlorophenylthiazolidine was filtered off, washed with water on the filter, dried and recrystallized from 80% alcohol; the m. p. was 48.5-49°. The yield was 1.94 g (90.5%).

The 2-methyl-3-p-chlorophenylthiazolidine was readily soluble in anhydrous alcohol, acetone and dichloroethane, difficultly soluble in ether and insoluble in water.

Found %: C 55.95, 55.81; H 5.64, 5.60; N 6.68, 6.55. $C_{10}H_{12}NSCl$. Calculated %: C 56.21; H 5.66; N 6.86.

2-Ethyl-3-p-chlorophenylthiazolidine. 1.88 g (0.01 mole) of N-(β-mercaptoethyl)-p-chloroaniline in 10 ml of anhydrous alcohol was mixed with 5.8 g (0.1 mole) of propionaldehyde; the mixture gave off heat strongly. The unchanged propionaldehyde and alcohol were distilled off in vacuum to leave a residue of 2-ethyl-3-p-chlorophenylthiazolidine which crystallized; m. p. 72-72.5° (from 80% alcohol). The yield was quantitative.

The 2-ethyl-3-p-chlorophenylthiazolidine was readily soluble in anhydrous alcohol, ether, acetone, benzene and dichloroethane, and insoluble in water.

Found %: C 57.79, 57.77; H 6.19, 6.34; N 5.78, 5.91. $C_{11}H_{14}NSCl$. Calculated %: C 58.00; H 6.20; N 6.15.

2-Propyl-3-p-chlorophenylthiazolidine. 1.88 g (0.01 mole) of N-(β-mercaptoethyl)-p-chloroaniline in 10 ml of anhydrous alcohol was mixed with 7.2 g (0.1 mole) of butyraldehyde; the mixture gave off heat strongly. When the unchanged butyraldehyde and alcohol had been distilled off in vacuum, the residual yellow oil crystallized after standing for 3 days in the cold. The crystals of 2-propyl-3-p-chlorophenylthiazolidine were quickly pressed out on a porous plate, dried and recrystallized from 80% alcohol; m. p. 32-32.5°. The yield was quantitative.

The 2-propyl-3-p-chlorophenylthiazolidine was readily soluble in anhydrous alcohol, ether, acetone, benzene and dichloroethane, and insoluble in water.

Found %: C 59.84, 59.70; H 6.63, 6.77; N 6.18, 6.20. $C_{12}H_{16}NSCl$. Calculated %: C 59.85; H 6.69; N 5.82.

2-Phenyl-3-p-chlorophenylthiazolidine. A mixture of 1.88 g (0.01 mole) of N-(β-mercaptoethyl)-p-chloroaniline and 5.3 g (0.05 mole) of benzaldehyde in 15 ml of anhydrous alcohol was left to stand at room temperature for 72 hours. The colorless, crystalline precipitate of 2-phenyl-3-p-chlorophenylthiazolidine was filtered off, washed with alcohol, dried and recrystallized from an alcohol – benzene mixture (5:1); m. p. 113.5-114°. The yield was 2.40 g (87%).

The 2-phenyl-3-p-chlorophenylthiazolidine was readily soluble in ether, benzene and dichloroethane, difficultly soluble in alcohol and acetone, and insoluble in water.

Found %: C 65.76, 65.67; H 5.47, 5.49; N 5.00, 5.08. $C_{15}H_{14}NSCl$. Calculated %: C 65.35; H 5.12; N 5.08.

3-p-Chlorophenylthiazolidone-2. 10 ml (0.02 mole) of a 20% solution of phosgene in toluene was quickly added to a solution of 1.88 g (0.01 mole) of N-(β-mercaptoethyl)-p-chloroaniline in 5 ml of toluene; the mixture gave off heat strongly. When the toluene had been distilled off in vacuum (on a water bath), the dark crystalline residue was dissolved in anhydrous alcohol and decolorized by boiling with charcoal. After filtering and cooling the solution, we obtained colorless crystals of 3-p-chlorophenylthiazolidone-2; m. p. 88-88.5°. The yield was 1.53 g (71.5%).

The 3-p-chlorophenylthiazolidone-2 was readily soluble in ether, benzene, acetone and dichloroethane, difficultly soluble in alcohol, and insoluble in water.

Found %: C 50.34, 50.24; H 3.52, 3.70; N 6.37, 6.52. C_9H_8ONSCl. Calculated %: C 50.58; H 3.77; N 6.56.

3-p-Chlorophenylthiazolidinethione-2. 3.04 g (0.04 mole) of carbon disulfide was added to a solution of 3.76 g (0.02 mole) of N-(β-mercaptoethyl)-p-chloroaniline and 1.12 g (0.02 mole) of potassium hydroxide in 10 ml of anhydrous alcohol. The mixture was boiled for 8 hours, the unchanged carbon disulfide and alcohol were distilled off and the orange, crystalline residue was washed with water until it was colorless and then it was recrystallized from alcohol; m. p. 139.5-140°. The yield was 2.01 g (43.5%).

The 3-p-chlorophenylthiazolidinethione-2 was readily soluble in acetone, benzene and dichloroethane, difficultly soluble in alcohol and ether, and insoluble in water.

Found %: C 47.24, 47.40; H 3.73, 3.70; N 5.95, 5.90. $C_9H_8NS_2Cl$. Calculated %: C 47.06; H 3.51; N 6.10.

3-p-Chlorophenylthiazolidone-2 from 3-p-chlorophenylthiazolidinethione-2. A mixture of 0.07 g (0.0003 mole) of 3-p-chlorophenylthiazolidinethione-2 and 0.15 g (0.0007 mole) of mercuric oxide in 2 ml of glacial acetic acid was boiled for 3 hours, the hot solution filtered, the acetic acid distilled off in vacuum, the crystalline residue dissolved in hot, anhydrous methyl alcohol and the insoluble material filtered off from the solution. After cooling the solution, we obtained 0.02 g of 3-p-chlorophenylthiazolidone-2; m. p. 88-88.5°. A mixed melting point with authentic 3-p-chlorophenylthiazolidone-2 was not depressed.

SUMMARY

1. Ethylene sulfide reacted with p-chloroaniline to give N-(β-mercaptoethyl)-p-chloroaniline, which could be oxidized with iodine to give β,β'-di-(p-chlorophenylamino)-diethyl disulfide dihydroiodide.

2. N-(β-Mercaptoethyl)-p-chloroaniline condensed readily with aliphatic and aromatic aldehydes (formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde and benzaldehyde), phosgene and with carbon disulfide. In this way we prepared 3-p-chlorophenyl-, 2-methyl-3-p-chlorophenyl-, 2-ethyl-3-p-chlorophenyl-, 2-propyl-3-p-chlorophenyl- and 2-phenyl-3-p-chlorophenylthiazolidine, which have not been described in the literature, and 3-p-chlorophenylthiazolidone-2 and 3-p-chlorophenylthiazolidinethione-2.

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SYNTHESIS OF THIAZOLIDONE DERIVATIVES OF BIOLOGICAL INTEREST

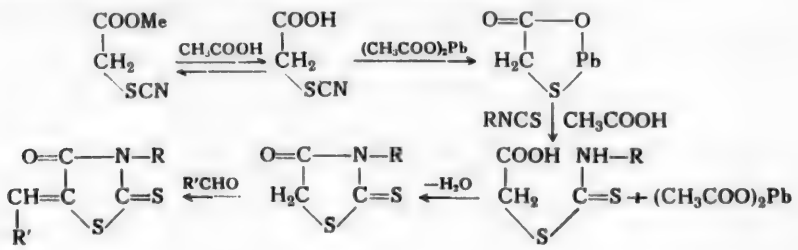
VII. SYNTHESIS OF N-SUBSTITUTED RHODANINE DERIVATIVES STARTING FROM THIOCYANOACETATES

V. G. Zubenko and N. M. Turkevich

N-Substituted rhodanine derivatives have lately acquired some value due to their fungicidal properties [1]. Some of them have been used for the preparation of photosensitizers [2, 3]. The methods of preparing these substances described to now in the literature have a number of disadvantages. The starting materials for the synthesis of these substances are derivatives of dithiocarbamic acid [4], thioglycolic acid, mustard oils [5] and thiocarbonyl-bisthioglycolic acid [6].

From a series of investigations, we found that the most convenient starting material for the synthesis of rhodanine N-derivatives were salts of thiocyanoacetic acid, which are completely stable and may be readily prepared [7] by treating the sodium salt of monochloroacetic acid with potassium thiocyanate.

The method we proposed may be represented by the scheme:



We used glacial acetic acid as the condensing agent for the conversion of thiocyanoacetates into thiocyanoacetic acid and to bind the ammonia formed.

Hydrolysis of the thiocyano group was initiated by small amounts of water found in the acetic acid and in crystalline lead acetate.

More water molecules were freed by the subsequent formation of the thiazolidine ring and condensation of aldehydes at position 5.

Lead acetate was the catalyst for converting the thiocyanoacetic acid to thioglycolic acid, which reacted with mustard oils to give derivatives of thiocarbaminylthioglycolic acid. The latter were very readily dehydrated by boiling in glacial acetic acid to form a thiazolidine ring.

The reaction was carried out with phenyl- and allylmustard oils and we established the possibility of introducing aldehydes into the condensation at the same time. The reactions were carried out with benzaldehyde, salicylaldehyde, m-nitrobenzaldehyde, p-nitrobenzaldehyde, p-acetaminobenzaldehyde, naphthaldehyde, hydroxynaphthaldehyde, cinnamaldehyde and furfurol. Thus we prepared, in one stage, rhodanine derivatives substituted in the 3 and 5 positions in 63-100% yields.

EXPERIMENTAL

N-Phenylrhodanine and N-allylrhodanine. 20 mmoles of thiocyanoacetate, 20 mmoles of phenylmustard oil, 10 ml of glacial acetic acid and 0.5 g of lead acetate were heated on a boiling water bath until the evolution of carbon dioxide ceased (about 30 minutes). After about 10 minutes, the solution initially formed deposited a dark brown precipitate of the condensation product, containing a small amount of PbS impurity. The reaction mixture was diluted with water and the precipitate filtered off, dried and recrystallized from glacial acetic acid.

Substance	Yield (in %)	Melting point	Solvent for recrystallization	Nitrogen content (in %)		Remarks
				found	calc.	
N-Phenylrhodanine	90.6	192—193°	Acetic acid	6.55	6.99	
N-Phenyl-5-benzylidenerhodanine	75.7	187—189	The same	4.61	4.71	
N-Phenyl-5-o-hydroxybenzylidenerhodanine	80.6	179—180	"	4.60	4.47	
N-Phenyl-5-m-nitrobenzylidenerhodanine	87.6	243.5	Acetic anhydride	8.15	8.18	
N-Phenyl-5-p-nitrobenzylidenerhodanine	95	263—264	The same	8.19	8.18	
N-Phenyl-5-p-acetaminobenzylidenerhodanine	63.8	> 284	Acetic acid	7.82	7.91	Found %: C 59.54, H 3.97. Calculated %: C 61.00, H 3.98
N-Phenyl-5-cinnamylidenerhodanine	74.8	222	The same	4.29	4.33	
N-Phenyl-5-α-naphthylidenerhodanine	100	145—147	"	3.93	4.03	Found %: C 68.54, H. 3.84. Calculated %: C 69.14, H 3.77.
N-Phenyl-5-furfurylidenerhodanine	78.4	183	"	4.80	4.88	
N-Allylrhodanine	86.7	42	Ether	8.15	8.03	
N-Allyl-5-benzylidenerhodanine	85.7	143—144	Acetic acid	5.40	5.36	
N-Allyl-5-o-hydroxybenzylidenerhodanine	81.2	179—180	The same	5.04	5.05	
N-Allyl-5-m-nitrobenzylidenerhodanine	73.5	148	"	9.10	9.14	
N-Allyl-5-cinnamylidenerhodanine	64.9	176—178	"	4.93	4.87	
N-Allyl-5-α-naphthylidenerhodanine	87.0	111—113	Ethyl alcohol	4.59	4.49	Found %: C 65.63, H 4.26. Calculated %: C 65.56, H 4.21
N-Allyl-5-8-hydroxy-α-naphthylidenerhodanine	92.3	195—196	Acetic acid	4.31	4.27	Found %: C 61.68, H 3.98. Calculated %: C 62.36, H 4.00
N-Allyl-5-furfurylidenerhodanine	69.7	101—102	The same	5.48	5.57	

The synthesis of N-allylrhodanine was carried out similarly and in this case the condensation product was a brown oil, which crystallized from ether as light brown crystals.

The condensation products of N-phenyl- and N-allylrhodanines with aldehydes. Equimolecular amounts (20 mmoles each) of thiocyanoacetate, mustard oil and aldehyde were boiled under reflux with 15 ml of glacial acetic acid in the presence of 1.0 g of lead acetate until the evolution of carbon dioxide ceased (15-60 minutes). The initially formed solution deposited first the intermediate product, which again dissolved in the acetic acid after some time. In almost all the experiments, the condensation product precipitated after 10-15 minutes.

All the arylidene derivatives of N-phenyl- and N-allylrhodanine, which we prepared were of varying shades of yellow, except the hydroxynaphthylidene derivative of N-allylrhodanine, which was red.

The substances we synthesized are listed in the Table. The results of C, H and N determinations are given for the substances, which have not been described in the literature up to now. The melting points of all the other substances agreed with literature data [5, 6, 8-10].

SUMMARY

1. Condensation of thiocyanoacetates with phenyl- or allylmustard oils in a glacial acetic acid medium in the presence of lead acetate gave N-phenyl- and N-allylrhodanines, respectively.

2. Condensation of thiocyanoacetates with phenyl- or allylmustard oil in the presence of aromatic aldehydes and lead acetate gave 5-arylidene derivatives of N-phenyl- and N-allylrhodanines, respectively, in one stage.

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THE NITRATION OF PHTHALONES

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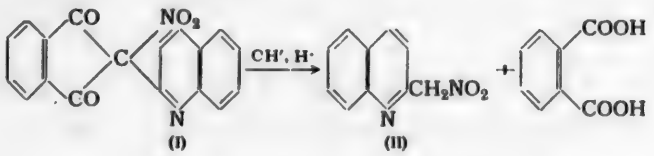
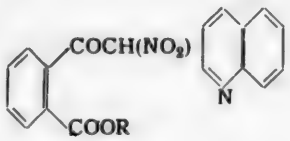
Previous papers describe the nitration of quinophthalone and the hydrolytic decomposition of the nitration product (I) to 2-nitromethylquinoline (II) [1].

Later, this reaction was extended to quinaldine homologs and a convenient method was developed for the alcoholysis of nitroquinophthalone (I) to esters of α-nitro-α-(2-quinolyl)-acetophenone-o-carboxylic acid (III) [2].

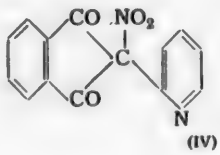


(I) (II)



(III)

The general applicability of this reaction is shown in this paper using as examples phthalones of 2-methylpyridine and 2-methylbenzthiazole. Nitropyrophthalone (IV) and nitrobenzthiazophthalone (V) were obtained under very mild conditions and by an extremely simple method.



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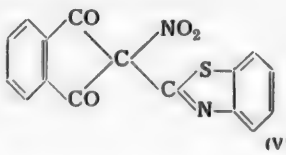
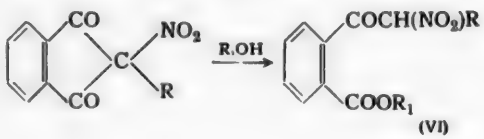


(V)

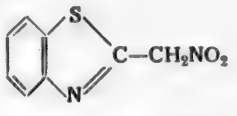
Boiling in alcohols or treatment with alcoholates smoothly converted these compounds into the corresponding esters of α-nitro-α-substituted acetophenone-o-carboxylic acids (VI) by the reaction



(VI)

Thus, we obtained good yields of esters with the 2-benzthiazolyl (R_1 = CH_3 and C_2H_5) radical and 2-pyridyl (R_1 = CH_3, C_2H_5) radical.

Solution of nitrophthalones in alkalis with subsequent acidification of the alkaline solutions gave, in both cases, the corresponding nitromethanes with heterocyclic substituent (VII, VIII).



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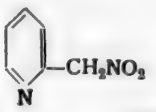

(VIII)

However, we could not purify 2-nitromethylpyridine, which was isolated in liquid form.

The structure of 2-nitromethylbenzthiazole, obtained in good yields in the form of yellow crystals, was proved by converting it to benzthiazole-2-carboxylic acid by sulfuric acid treatment by the general reaction for primary nitro compounds.

In connection with this, we consider as questionable the paper by A. I. Kiprianov and E. D. Smaznaya-Ilyina [3], in which they report the preparation of 2-nitromethylbenzthiazole from o-aminothiophenol and nitroacetic ester and do not give convincing data that would confirm the structure of the material.

EXPERIMENTAL

Nitrobenzthiazophthalone (V). a) Benzthiazophthalone was prepared in 21% yield by heating 37 g of 2-methylbenzthiazole and 37 g of phthalic anhydride on a sand bath for 13 hours and then purifying the phthalone by boiling it with alcohol, in which it is insoluble. M. p. 350°.

Found %: N 5.09. $C_{16}H_9O_2NS$. Calculated %: N 5.02.

Benzthiazophthalone dissolves very slightly on boiling in glacial acetic acid, alcohol, acetone, chloroform, carbon tetrachloride and benzene. It crystallizes readily from nitrobenzene and after recrystallization from the latter, the melting point remains at 350°.

b) For the preparation of the nitroderivative, 14.5 g of the phthalone was carefully powdered and a mixture of 35 ml of nitric acid (d 1.47) and 100 ml of acetic acid was poured onto it. After shaking it for 10 minutes, we separated off the precipitate, washed it with alcohol and dried it in the air. We obtained 12 g of 2-nitro-2-(2'-benzthiazolyl)-indanedione-1,3 (V) with m. p. 145-146°. After recrystallization from glacial acetic acid, the material had the same melting point. The yield was 71%.

Found %: N 8.46. $C_{16}H_8O_4N_2S$. Calculated %: N 8.64.

Esters of α-nitro-α-(2-benzthiazolyl)-acetophenone-o-carboxylic acid (VI). a) 1 g of 2-nitro-(2'-benzthiazolyl)-indanedione-1,3 (V) was treated with 20 ml of a 3% solution of sodium methylate in methanol. The substance dissolved at room temperature to give an orange solution. After filtration and acidification of the filtrate with dilute acetic acid, the methyl ester of α-nitro-α-(2-benzthiazolyl)-acetophenone-o-carboxylic acid (VI, R = 2-benzthiazolyl, R_1 = CH_3) was precipitated. The yield was 0.7 g. The m. p. was 192-193°. After recrystallization from acetone, the material had m. p. 193-194°.

Found %: N 8.04. $C_{17}H_{12}O_5N_2S$. Calculated %: N 7.80.

b) The ethyl ester (VI, R = 2-benzthiazolyl, R_1 = C_2H_5) was prepared similarly, using sodium ethylate in anhydrous ethanol. The yield was 0.45 g. The m. p. was 186-187° from benzene.

Found %: N 7.47. $C_{18}H_{14}O_5N_2S$. Calculated %: N 7.57.

2-Nitromethylbenzthiazol (VII). 13.5 g of nitrobenzthiazophthalone (V) was treated with 250 ml of 10% sodium hydroxide, the mixture heated for half an hour on a water bath to 60°, diluted with an equal volume of water and kept at the same temperature for some time longer. The solution was filtered and the filtrate acidified with dilute acetic acid. The weight of the yellow precipitate was 7 g, decomp. point 123-124°. For purification, the material was dissolved in aqueous bicarbonate, precipitated with acetic acid and recrystallized from alcohol. It formed lustrous, yellow plates. It was characteristic that the substance melted with decomposition over a range of 1-2° in each case, but the decomposition point was not always constant and fell in the interval 120-130° and sometimes even higher.

Found %: N 14.27. $C_8H_6O_2N_2S$. Calculated %: N 14.43.

3 g of impure 2-nitromethylbenzthiazole was treated with 35 ml of 80% sulfuric acid and heated for 45 minutes at 90-97°. The brown solution was cooled, diluted with water, and the separated precipitate was treated with a small amount of sodium carbonate. The precipitated sodium benzthiazole-2-carboxylate was recrystallized from water, dissolved in warm water and the free acid liberated by acidification. We obtained 1 g (36%) of benzthiazole-2-carboxylic acid. The m. p. was 105-106°. A mixture with an authentic sample, prepared by Reissert's method [4], melted without depression at 105-106°.

Nitropyrophthalone (IV). a) The α-picoline fraction of coal tar from one of the Donbas factories was redistilled. The product, which boiled in the range 125-130°, was used as the starting material for the preparation of pyrophthalone. The latter was prepared by heating phthalic anhydride with α-picoline for 20 hours at 210-220°. The yield was 58-61%. The m. p. was 277-280°.

Found %: N 6.61. $C_{14}H_9O_2N$. Calculated %: N 6.28.

b) 5.5 g of carefully powdered phthalone was treated with 50 ml of nitric acid (d 1.35) and the mixture vigorously shaken for several seconds and poured into water. The precipitate was quickly separated and washed with water. We obtained 3.65 g (55%) of the substance (IV) with m. p. 147-148°. After recrystallization from benzene, the substance had m. p. 151-152° (with decomp.).

Found %: C 62.95; H 3.20; N 10.46. $C_{14}H_8O_4N_2$. Calculated %: C 62.69; H 2.98; N 10.45. Found: M 259.4 (ebullioscopically in acetone); calc. 268.0.

Esters of α-nitro-α-(2-pyridyl)-acetophenone-o-carboxylic acid (VI). a) For the preparation of the methyl ester (VI, R = 2-pyridyl, $R_1 = CH_3$), 1 g of the nitrodiketone (IV) was treated with 20 ml of 3% sodium methylate in methanol. On being shaken, the substance very quickly dissolved to give a bright yellow solution. After acidification with dilute acetic acid and standing for a short time, the solution deposited prismatic yellow crystals. We obtained 0.9 g of a substance with m. p. 139-140°. The yield was 78%.

Found %: C 60.30; H 4.01; N 9.27. $C_{15}H_{12}O_5N_2$. Calculated %: C 60.00; H 4.00; N 9.33.

The same substance may be prepared without using sodium methylate by simply by boiling in methanol.

7.2 g of nitropyrophthalone with m. p. 147-148° was boiled for 30 minutes in 100 ml of methanol. On cooling, 5.3 g of crystals with m. p. 141-142° was deposited. A mixture with the ester obtained previously melted without depression.

b) For the preparation of the ethyl ester (VI, R = 2-pyridyl, $R_1 = C_2H_5$), the nitrodiketone (IV) was heated for half an hour with anhydrous ethanol. On standing overnight, the solution deposited a yellow crystalline powder with m. p. 109-110°.

Found %: C 61.52; H 3.82; N 9.15. $C_{16}H_{14}O_5N_2$. Calculated %: C 61.15; H 4.44; N 8.91.

The same product may be prepared from pyrophthalone, without isolating the intermediate nitrodiketone.

10 g of pyrophthalone was dissolved in 50 ml of nitric acid (d 1.36). The substance very quickly dissolved with the evolution of oxides of nitrogen. The solution was diluted with water and the precipitate of crude nitro product pressed on a filter and heated for 3 minutes in alcohol. The mixture was cooled, diluted with a little water and left to stand overnight. After drying, the substance had m. p. 103-105° and was dissolved in aqueous ammonia, liberated with hydrochloric acid and recrystallized from alcohol. The weight was 2.4 g. The m. p. was 109-110°. A mixture with the product obtained previously melted without depression.

Attempted preparation of 2-nitromethylpyridine (VIII). 20 g of nitropyrophthalone (IV) (m. p. 147-148°) was carefully powdered and treated with 80 ml of 10% aqueous sodium hydroxide solution. The mixture was kept at room temperature for 3 hours and vigorously stirred mechanically. The dark red liquid was diluted with water and filtered. 1 g of insoluble material remained. The filtrate was acidified with dilute acetic acid and this produced a finely crystalline precipitate of phthalic anhydride. The weight of air-dried material was 8 g and the m. p. 125-128°. After recrystallization from carbon tetrachloride, the substance formed long needles with m. p. 129-130°. A mixture with an authentic preparation melted without depression. After removal of the phthalic anhydride, the filtrate was treated with chloroform and the chloroform extracts washed with bicarbonate solution and dried over sodium sulfate. The solvent was distilled off and the last traces of it were removed in vacuum. As a result we obtained a dark oil, which was probably impure 2-nitromethylpyridine, which could not be purified as it decomposed during vacuum distillation.

Found %: N 16.31. $C_8H_8O_2N_2$. Calculated %: N 20.28.

After recrystallization from alcohol, the picrate had m. p. 152-153°.

Found %: N 18.71. $C_{12}H_9O_9N_5$. Calculated %: N 19.07.

The substance was not examined further.

SUMMARY

The nitration of phthalones of 2-methylbenzthiazole and 2-picoline was studied; nitrophthalones were prepared and their hydrolysis and alcoholysis studied.

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THE REACTIONS OF PYRIDINIUM SALTS

I. THE SYNTHESIS OF CHLORODINITROPHENYLATES OF SUBSTITUTED PYRIDINE BASES

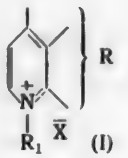
A. F. Vompe and N. F. Turitsyna

In the study of the nature of heterocyclic bonds, reactions involving the rupture of these bonds are of exceptionally great interest. One of the most outstanding examples of such a reaction is the cleavage of the pyridine ring, which occurs under the effect of basic substances, for example aromatic amines, on pyridinium salts (I; R = H), containing electronegative radicals (in particular, the 2,4-dinitrophenyl radical at the ring nitrogen [1]).

In spite of the considerable number of papers devoted to the cleavage of the pyridine ring, up to now almost nothing has been known on the effect of substituents (in the ring and at the ring nitrogen atom) of an amine nature and of other factors on the tendency of the pyridine ring to cleave and on the course of the reaction. The formation of pyridinium salts (I), containing substituents in the pyridine nucleus likewise has not been studied.

In connection with this, we first investigated the formation of chloro-(2,4-dinitro)phenylates of substituted pyridines (cf. [2]).

As a rule, the pyridine bases were reacted with 2,4-dinitrochlorobenzene by heating an equimolecular mixture of the components in dry acetone or without solvent. Under these conditions, chlorodinitrophenylates of substituted pyridines of the general formula ($R_1 = C_6H_3(NO_2)_2$; X = Cl), were readily formed.



(I)

where R: β-CH_3, OH, OCH_3, $NHCOCH_3$, $N(CH_3)_2$, I, $CON(C_2H_5)_2$; γ-$NHCOCH_3$, NHC_6H_5; R_1: CN, $C_6H_4(NO_2)_2$ etc. X: anion

Under the usual experimental conditions (heating on a water bath under reflux) dinitrochlorobenzene could not be added to β-chloropyridine (cf. [3]), β-bromopyridine, β-nitropyridine and ethyl nicotinate. The same conditions gave only a very small yield of the chlorodinitrophenylate of ethyl isonicotinate.

Likewise, very low yields of chlorodinitrophenylates of β-bromopyridine and ethyl nicotinate were obtained by heating the components in sealed tubes, while β-nitropyridine did not add dinitrochlorobenzene even under relatively drastic conditions (long heating in a sealed tube at 130°).

Thus, on introducing substituents of a strongly electronegative character into the β- and γ-positions of the pyridine ring, the tendency for the ring nitrogen to pass into a tetravalent, positively-charged state decreased. This conclusion agrees with the observations of A. E. Chichibabin and A. V. Kirsanov [4], who found that the introduction of a nitro group into the β-position of the pyridine ring strongly decreased the tendency of the ring nitrogen to add to methyl iodide. In exactly the same way, Laidler [5] showed that the introduction of a $COOC_2H_5$ group into the β-position of pyridine was accompanied by a rise in the activation energy of methiodide formation.

It was to be expected that a decrease in the electronegative nature of the substituent in the pyridine nucleus (for example in going from Cl and Br to I or from the $COOC_2H_5$- to the $CON(C_2H_5)_2$- group) would facilitate the formation of chlorodinitrophenylates.

In fact, dinitrochlorobenzene added quite readily to β-iodopyridine and the diethylamide of nicotinic acid on heating on a water bath.

In order to elucidate the effect of introducing electropositive substituents into the β-position or γ-position of the pyridine ring on the formation of the chlorodinitrophenylate (I), we investigated the reaction of the appropriate pyridine bases with dinitrochlorobenzene in an acetone solution at 17-19° (with an equimolecular ratio of the components). The reaction time and initial concentrations (c) of the reacting substances were varied. For comparison we investigated the reaction of dinitrochlorobenzene with pyridine and the diethylamide of nicotinic acid.

The yields of chlorophenylates of the diethylamide of nicotinic acid, pyridine and γ-acetamino- β-dimethylamino- and γ-phenylaminopyridine were, after 22 hours (c = 0.25 M): 0, 1.8, 17.9, 26.1, 60.8%,* and after 56 hours: 0, 3.5, 35.8, 52.3 and 77.7%,* respectively.

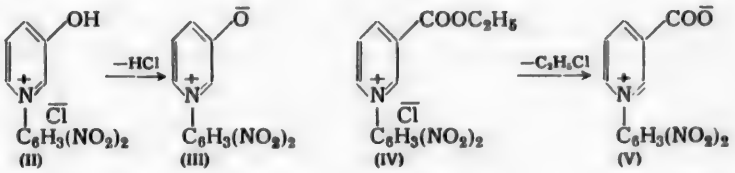
Under these conditions, β-acetaminopyridine and β-iodopyridine did not form addition products.

When the reaction was carried out in more concentrated solutions (c = 1 M), the yields of chlorodinitrophenylates of the diethylamide of nicotinic acid, pyridine and β-dimethylaminopyridine (13%) were, after 56 hours: 2.6, 17.7 and 84.7%, respectively.

Thus, as was to be expected, the introduction of an electropositive substituent into the β- or γ-position of the pyridine ring considerably accelerated the formation of a quaternary salt.

On heating ethyl nicotinate with dinitrochlorobenzene in a sealed tube at 100-130°, we observed the formation of two substances. One was the chlorodinitrophenylate mentioned above (m. p. 120°). The second had very different properties and melting point (230°) from those of chlorodinitrophenylate. The elementary analysis data for the second compound are quite similar to the formula of diethyl dipyridyldicarboxylate dihydrochloride. However, this substance was not examined in more detail.

The instability of the chlorodinitrophenylate of β-hydroxypyridine (II) should be noted, as it readily eliminates a molecule of hydrogen chloride to form a betaine (III).



This phenomenon explains why the analysis data (high nitrogen and low halide content) of crystallized chlorodinitrophenylate differs from theory.

The betaine (III) could be isolated by treating an aqueous solution of the chlorodinitrophenylate with sodium bicarbonate. The compound is readily soluble in dilute alkalis and acids.

When treated with picric acid the chlorodinitrophenylate (II) gave the quite stable β-hydroxypyridine dinitrophenylpicrate.

Heating the chlorodinitrophenylate of ethyl nicotinate (IV) (above its melting point) apparently eliminated the alkyl halide (at 126-128° bubbles of gas were evolved and at 140-160° the substance in the capillary again crystallized). One can assume that the N-dinitrophenyl analog of trigonelline (V) was thus formed.

* 0.1 M solutions of the components were reacted in the case of γ-phenylaminopyridine.

Addition of sodium bicarbonate to an aqueous solution of γ-phenylaminopyridine chlorodinitrophenylate gave N-dinitrophenyl-γ-pyridone anil. This compound readily added hydrogen chloride to form the original chlorodinitrophenylate.

α- and γ-picolines reacted with dinitrochlorobenzene to form dyes. It is interesting that on reacting γ-picoline with dinitrochlorobenzene (without solvent) the mixture noticeably evolved heat. The dye formed was of a blue-violet color.

It is quite probable that the first stage in these reactions is the formation of the corresponding addition products, which must have exceptionally active methyl groups. In this case, due to the great lability of the hydrogens in these groups, intermolecular reactions are possible involving the cleavage of the pyridine ring (cf. [6]). The nature of the colored compounds was not investigated more thoroughly.

We could not add dinitrochlorobenzene to α-methoxypyridine by heating the component mixture in acetone or without solvent. The reason for such a sharp decrease in reactivity was not clear. This phenomenon could be explained either by the low basicity of α-methoxypyridine (cf. [7]) or by steric hindrance (see, for example [8]).

EXPERIMENTAL

Pyridine Bases

β-Picoline was prepared by purifying the technical product (fraction with b. p. 141.7-142.7°) by heating it with benzaldehyde and fused zinc chloride in an autoclave. The β-picoline isolated from the reaction mixture was futher purified via the picrate. The b. p. was 143-143.5°. The melting point of the picrate was 147.5-149° (cf. [9]).

β-Hydroxypyridine was prepared by fusing the ammonium salt of pyridine-β-sulfonic acid with 4 times its weight of potassium hydroxide in a silver crucible on an oil bath (170-178°, 4 hours). The yield was 76 % (cf. [10]). The m. p. was 126.5-127.5° (cf. [27]).

β-Methoxypyridine was prepared by heating β-bromopyridine with a solution of sodium methylate in a rotating autoclave (140-153°, 40 hours) (cf. [11]). It was a colorless liquid with a pyridine-like smell. The b. p. was 177-179°. Literature data: b. p. 179° [11]. The picrate had m. p. 128-129°.

Found %: N 16.42. $C_{12}H_{10}O_8N_4$. Calculated %: N 16.57.

β-Acetaminopyridine was prepared by acetylating β-aminopyridine with acetic anhydride in a benzene solution (cf. [12]). It formed colorless plates (from benzene). The m. p. was 133-134°. Literature data: m. p. 133° [12].

β-Dimethylaminopyridine was prepared by treating a solution of β-aminopyridine in 1 N sulfuric acid with formaldehyde and zinc dust. The yield was 48.4% (cf. [13]). The light yellow liquid had b. p. 106-109° (6.5-7 mm). Literature data: b. p. 108-110° (12 mm) [13]. The picrate formed yellow prisms (from ethyl alcohol) with m. p. 174-175°

Found %: N 19.82, 19.70. $C_{13}H_{13}O_7N_5$. Calculated %: N 19.95.

β-Nitropyridine. The m. p. was 41° (cf. [14]). The picrate formed yellow prisms (from ethyl alcohol). The m. p. was 117°

Found %: N 19.81. $C_{11}H_7O_9N_5$. Calculated %: N 19.83.

β-Chloropyridine was prepared by Gatterman's method from β-aminopyridine, which was diazotized in hydrochloric acid [15]. The b. p. was 148-149° (corresponding with literature data [15]). The picrate had m. p. 145°.

β-Bromopyridine was prepared by brominating pyridine hydrochloride in the presence of mercuric chloride at 210-235° [16]. The yield varied from 20-30% (calculated on the reacted pyridine). At the same time

a considerable amount of 3,5-dibromopyridine was obtained. Separation of the two bases by fractional distillation, as recommended by Maier-Bode, was extremely difficult. After a series of experiments, we arrived at a simpler and more reliable method of separation: the solution was acidified with hydrochloric acid and the β,β'-dibromopyridine (almost colorless leaves with m. p. 110°) was steam distilled off. Then the liquid was made alkaline and the β-bromopyridine extracted from it with ether. The β-bromopyridine obtained from the ether solution had a sharp boiling point (175°) (cf. [17]), while Maier-Bode reported b. p. 165-180° for this base. The picrate formed bright yellow prisms with m. p. 153°. The picrolonate formed light yellow needles. The m. p. was 151°.

β-Iodopyridine was prepared by diazotizing β-aminopyridine [18]. The yield was 52.6%. The crystals were almost colorless. The m. p. was 52-53°. Literature data: m. p. 50° [18]. The picrate formed dark yellow, prismatic crystals with m. p. 153°.

Ethyl nicotinate was prepared by heating nicotinic acid with absolute ethyl alcohol and concentrated acid. The b. p. was 99° (7 mm); 223-224°. Literature data: b. p. 223-224° [20].

The diethylamide of nicotinic acid: b. p. 175° (25 mm). The melting point of the picrate was 123.5°. Literature data: m. p. 122-123° [19].

γ-Acetaminopyridine was prepared by acetylating γ-aminopyridine with acetic anhydride [21]. It crystallized from benzene. The m. p. was 149-150°. Literature data: m. p. 150° [21].

γ-Phenylaminopyridine was prepared by treating γ-pyridylpyridinium dichloride with aniline in ethyl alcohol [23]. The yield was 23.1%.

It formed almost colorless, lustrous needles. The m. p. was 179-180°. Literature data: m. p. 175° [23].

Ethyl isonicotinate. B. p. 215-216°. Literature data: b. p. 218° [22]; 219-220° [24].

The picrate formed bright yellow prisms (from ethyl alcohol). M. p. 120-121.5°.

Found %: N 14.36. $C_{14}H_{12}O_9N_4$. Calculated %: N 14.74.

Synthesis of Chlorodinitrophenylates

Pyridine chloro(2,4-dinitro)phenylate. The direct action of dinitrochlorobenzene on pyridine in the absence of solvent or in an alcohol solution, gave a strongly colored product with a low melting point (cf. [25]).

Carrying out the reaction in acetone gave pyridine chlorodinitrophenylate with a high melting point in almost quantitative yield.

40 g of 2,4-dinitrochlorobenzene was dissolved in 80 ml of acetone and 20 g of dry pyridine added to the solution. The light yellow liquid was heated to boiling (on a water bath) and boiled for 15 hours. Slightly yellow crystals gradually separated and these were washed on a filter with acetone and ether.

Heating the acetone solution further gave a little more material. The yield was 53.7 g (96.8%). The material formed slightly yellow needles (from ethyl alcohol). The m. p. was 190-191° (slow heating) (cf. [25]).

β-Picoline chloro(2,4-dinitro)phenylate. A solution of 4.04 g of 2,4-dinitrochlorobenzene and 1.84 g of β-picoline in 16 ml of dry acetone was heated on a water bath for 10 hours. The crystals isolated from the solution were washed on a filter with acetone and ether. The yield was 5.33 g (90.2%). The m. p. was 196-199°. After 2 recrystallizations from absolute ethyl alcohol (with charcoal), the material was obtained as almost colorless needles with m. p. 208-209°. Literature data: m. p. 206-210° [26]. The substance was soluble in water and slightly soluble in acetone.

Found %: N 14.26; Cl 12.24, 12.25. $C_{12}H_{10}O_4N_3Cl$. Calculated %: N 14.22; Cl 12.00.

Reaction of β-hydroxypyridine with 2,4-dinitrochlorobenzene. A mixture of 0.47 g of β-hydroxypyridine and 1.01 g of 2,4-dinitrochlorobenzene was heated on a water bath (90°) for 6 hours. The crystalline mass was washed with dry acetone and ether. The yield was 0.80 g. The m. p. was 180-185°. Two recrystallizations from ethyl alcohol gave slightly yellowish prisms with m. p. 193-194°. The material was quite difficultly soluble in water.

Found %: N 15.75; Cl 8.95, 8.64, 8.57. $C_{11}H_8O_8N_3Cl$. (see formula II). Calculated %: N 14.12; Cl 11.91. $C_{11}H_7O_5N_3$ (see formula III). Calculated %: N 16.09.

The N-(2,4-dinitrophenyl)picrate of β-hydroxypyridine was prepared by precipitation from the reaction solution of β-hydroxypyridine chlorodinitrophenylate (0.09 g) in hot ethyl alcohol (11 ml) with picric acid (0.08 g in 1 ml of ethyl alcohol). The weight of the picrate was 0.12 g (81.6%). The m. p. was 208-209° (after washing with boiling ethyl alcohol). The material formed fine, yellow crystals. It was quite difficultly soluble in ethyl alcohol.

Found %: N 17.09, 16.93. $C_{17}H_{10}O_{12}N_6$. Calculated %: N 17.14.

N-(2,4-dinitrophenyl)-β-hydroxypyridinium betaine. 0.148 g of the reaction β-hydroxypyridine chlorodinitrophenylate was dissolved in 4 ml of water with heating. Sodium bicarbonate (0.063 g) was added to the cooled solution and there was a vigorous evolution of carbon dioxide. On long standing, the solution gradually deposited yellowish crystals. They were washed with water and dried. The weight was 0.08 g (61.5%). The m. p. was 124°. Recrystallization from ethyl alcohol (with charcoal) gave slightly yellowish prisms with m. p. 128°. The substance was insoluble in cold water and readily soluble in dilute acids and alkalis. It did not contain halogen.

Found %: N 16.09, 16.30. $C_{11}H_7O_5N_3$. Calculated %: N 16.09.

β-Methoxypyridine chloro(2,4-dinitro)phenylate. 0.10 g of β-methoxypyridine and 0.18 g of 2,4-dinitrochlorobenzene were heated in 0.5 ml of dry acetone on a water bath (65-70°, 8 hours). The dark brown mass was dissolved in water (25 ml). The aqueous solution was shaken with ether and when the ether had been separated off, it was decolorized by heating with charcoal and evaporated in vacuum. The yield was 0.13 g (45.6%). The substance formed very hygroscopic, colorless crystals.

β-Acetaminopyridine chloro(2,4-dinitro)phenylate was prepared by heating a mixture of 2.72 g of β-acetaminopyridine and 4.05 g of 2,4-dinitrochlorobenzene in 22 ml of dry acetone on a water bath for 5 hours. After 24 hours, the crystals were filtered off and washed with acetone. The yield was 4.3 g (63.5%). The substance formed colorless prisms (from absolute ethyl alcohol). The m. p. was 183°. The substance contained alcohol of crystallization. It was soluble in water.

Found %: N 15.45, 15.38. $C_{13}H_{11}O_5N_4Cl \cdot {}^1/_2 C_2H_5OH$. Calculated %: N 15.50.

After drying in vacuum at 60-70°:

Found %: N 16.50, 16.40; Cl 10.24. $C_{13}H_{11}O_5N_4Cl$. Calculated %: N 16.55; Cl 10.48.

β-Dimethylaminopyridine chloro(2,4-dinitro)phenylate. 0.24 g of β-dimethylaminopyridine was added to a solution of 0.41 g of 2,4-dinitrochlorobenzene in 2 ml of dry acetone and the mixture kept for 56 hours at 17-19°. The yield was 0.55 g (84.7%). The substance formed lemon yellow plates (from a mixture of 1:1 absolute ethyl alcohol and acetone). The m. p. was 183-184.5°. The substance was soluble in water.

Found %: Cl 10.88, 11.00. $C_{13}H_{13}O_4N_4Cl$. Calculated %: Cl 10.92.

Reaction of β-chloropyridine and β-nitropyridine with 2,4-dinitrochlorobenzene. Equimolecular mixtures of the bases and 2,4-dinitrochlorobenzene were heated under reflux for 10 hours on a boiling water bath in the case of β-chloropyridine and for 24 hours in a sealed tube at 130° in the case of β-nitropyridine. In both experiments, aqueous extracts from the reaction mixtures did not give qualitative reactions for chlorodinitrophenylates (tests with sodium bicarbonate and with solutions of alkalis). On precipitating the ether extracts with picric acid, we obtained the picrates of the corresponding bases.

β-Bromopyridine chloro(2,4-dinitro)phenylate. A mixture of 2.02 g of dinitrochlorobenzene and 1.57 g of β-bromopyridine was heated in a sealed tube on a boiling water bath for 24 hours. The partly crystalline mass was treated with ether. The yield of chlorodinitrophenylate was 0.67 g (18.6%). The m. p. was 145°

(unchanged after recrystallization from absolute ethyl alcohol). The substance formed fine, colorless prisms. It was readily soluble in water and alcohol, more difficultly soluble in acetone and insoluble in ether. The aqueous solutions were extremely sensitive to the action of alkalis.

Found %: Cl 9.96, 9.97. $C_{11}H_7O_4N_3BrCl$. Calculated %: Cl 9.83.

The ether filtrate (after separation of the chlorodinitrophenylate) was precipitated with picric acid (2.64 g in 100 ml of ethyl alcohol). We collected 3.42 g (81.2%) of material. The light yellow needles (from ethyl alcohol) had m. p. 150°; they did not depress the melting point of β-bromopyridine picrolonate.

β-Iodopyridine chloro(2,4-dinitro)phenylate. A mixture of 2.04 g of β-iodopyridine and 2.02 g of dinitrochlorobenzene was ground in a mortar and heated on a boiling water bath for 14 hours. The solid mass was washed with ether. The yield was 3.55 g (87.2%). The m. p. was 178°. Washing the product with boiling acetone and recrystallizing it from ethyl alcohol raised the melting point to 180-181°. The colorless crystals were soluble in water and alcohol, slightly more difficultly soluble in acetone and insoluble in ether.

Found %: N 10.35. $C_{11}H_7O_4N_3ClI$. Calculated %: N 10.30.

Reaction of ethyl nicotinate with 2,4-dinitrochlorobenzene. 7.55 g of ethyl nicotinate and 10.12 g of dinitrochlorobenzene were heated in a sealed tube for 15 hours at 100° and for 46 hours at 130°. After treating the dark, semicrystalline mass with dry ether and acetone, we obtained 2.89 g of slightly yellowish crystals with m. p. 140-141°. Recrystallization from absolute ethyl alcohol (1:7) gave colorless prisms with m. p. 230° (0.94 g). They were soluble in water (the solutions contained halide ions) and insoluble in ether. The aqueous solutions did not become colored on adding alkalis.

Found %: Cl 19.18, 19.00, 19.05; C 51.59, 51.80; H 5.53, 5.52. $[NC_5H_3(COOC_2H_5)]_2 \cdot 2HCl$. Calculated %: Cl 19.01; C 51.46; H 4.86.

Ether was added to the alcohol filtrate from the crystallization to give yellowish crystals which were then washed with acetone, reprecipitated from alcohol with ether and dried to constant weight in vacuum at 60-70°. The weight was 1.74 g (9.8% calculated on the chlorodinitrophenylate of ethyl nicotinate). The m. p. was 120° (at 126-128° a gas was liberated, at 140-160°, the substance again crystallized and melted again at 199°). The substance formed colorless crystals. They were very readily soluble in water and alcohol, more difficultly soluble in acetone and insoluble in ether. The aqueous solutions were extremely sensitive to alkalis.

Found %: N 11.80, 11.67; Cl 10.01, 9.89. $C_{14}H_{12}O_6N_3Cl$. Calculated %: N 11.88; Cl 10.02.

Chloro(2,4-dinitro)phenylate of the diethylamide of nicotinic acid. 21.36 g of the diethylamide of nicotinic acid and 24.24 g of 2,4-dinitrochlorobenzene were heated on a boiling water bath for 6 hours. The crystalline mass was washed with dry acetone and dried in vacuum. The weight was 16.9 g (37%). The m. p. was 149°. The substance formed colorless leaves. It was readily soluble in water. It was soluble in ethyl alcohol, but recrystallization of the salt from absolute alcohol was unsuccessful due to its instability. Aqueous solutions (containing chlorine ions) were very sensitive to the action of even weak alkalis.

Found %: Cl 9.30, 9.38. $C_{16}H_{17}O_5N_4Cl$. Calculated %: Cl 9.32.

γ-Acetaminopyridine chloro(2,4-dinitro)phenylate. A solution of 0.82 g of γ-acetaminopyridine and 1.22 g of 2,4-dinitrochlorobenzene in 17 ml dry acetone was heated on a water bath at 50-60° (6 hours). After 20 minutes, the separation of crystals began. After heating, they were filtered off and washed with acetone. The weight was 1.45 g. The m. p. was 224° (unchanged after recrystallization from ethyl alcohol). The substance formed long colorless prisms (from ethyl alcohol). They contained alcohol of crystallization (determined by drying the substance in vacuum at 80-90°). The addition of ether to the filtrate gave a further 0.2 g of the salt with m. p. 217-219° (total yield 81.2%).

Found %: C_2H_5OH 6.92; N 15.46, 15.30, 15.53; Cl 10.19, 10.15. $C_{13}H_{11}O_8N_4Cl \cdot \frac{1}{2}C_2H_5OH$. Calculated %: C_2H_5OH 6.37; N 15.50; Cl 9.80.

γ-Phenylaminopyridine chloro(2,4-dinitro)phenylate. A solution of 1.02 g of γ-phenylaminopyridine and 1.22 g of 2,4-dinitrochlorobenzene in 27 ml of dry acetone was heated on a water bath at 50-80° for 6 hours. The crystals isolated were washed with acetone. The yield was 2.1 g (94.1%). The m. p. was 242° (unchanged after recrystallization from ethyl alcohol). The substance formed light yellow prisms. They were soluble in water and ethyl alcohol with a yellow color. The absorption maximum of an ethyl alcohol solution was at 310 mμ.

Found %: N 14.94; Cl 9.56, 9.51. $C_{17}H_{13}O_4N_4Cl$. Calculated %: N 15.04; Cl 9.52.

N-Dinitrophenyl-γ-pyridone anil. On adding sodium bicarbonate to an aqueous solution of 0.33 g of γ-phenylaminopyridine chlorodinitrophenylate, we observed the slow deposition of crystals of N-dinitrophenyl-γ-pyridone anil. The precipitate was washed on the filter with water and dried. The weight was 0.27 g (90.9%). The m. p. was 189°. After recrystallizing the product from ethyl alcohol, we obtained fine, reddish brown prisms with m. p. 192°. They were readily soluble in acetone, more difficultly soluble in ethyl alcohol (the absorption maximum of the solution was at 296 mμ) and benzene and insoluble in water. They dissolved in dilute hydrochloric acid with decolorization.

Found %: N 16.72. $C_{17}H_{12}O_4N_4$. Calculated %: N 16.66.

On shaking a suspension of 0.12 g of N-dinitrophenyl-γ-pyridone anil in 3 ml of 3% hydrochloric acid, the reddish brown crystals were converted into light yellow prisms of γ-phenylaminopyridine chlorodinitrophenylate (weight 0.1 g). The m. p. was 242°.

Reaction of ethyl isonicotinate with 2,4-dinitrochlorobenzene. A mixture of 0.75 g of ethyl isonicotinate and 1.02 g of 2,4-dinitrochlorobenzene was heated on a boiling water bath for 5 hours. The dark brown, viscous liquid was cooled and treated with dry ether (40 ml). The ether solution was filtered free from the greenish yellow, viscous residue and a picrate was isolated from the ether extract. The weight was 1.04 g (54.7%). The bright yellow prisms had m. p. 119-120° and did not depress the melting point of ethyl isonicotinate picrate.

The ether-insoluble residue (0.46 g) was mixed with water. The small residue was washed with water and dried. It consisted of yellow crystals. The weight was 0.07 g. The m. p. was 44-45°. The substance was readily soluble in ethyl alcohol and ether. It did not depress the melting point of 2,4-dinitrochlorobenzene. The aqueous solution was shaken with ether and then a picrate precipitated from it. The weight of the picrate was 0.46 g (16.9%, calculated on the N-dinitrophenylpicrate of ethyl isonicotinate). The material formed yellow crystals. It was very hygroscopic and rapidly deliquesced in air. It was recrystallized from absolute ethyl alcohol. The melting point (after drying in vacuum at 40°) was 59-61°.

Found %: N 15.36, 15.38. $C_{20}H_{14}O_{13}N_6$. Calculated %: N 15.39.

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SUMMARY

1. We investigated the reactions of a series of substituted pyridine bases with 2,4-dinitrochlorobenzene.

2. It was found that the introduction of electropositive substituents into the β- or γ-position of the pyridine ring facilitated, and electronegative substituents in the same positions hindered, the addition of a 2,4-dinitrochlorobenzene molecule to the ring nitrogen.

3. We describe the properties and certain reactions of chlorodinitrophenylates of substituted pyridine bases.

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THE CHEMISTRY OF XANTHOGENATES AND VISCOSE

VI. THE INTERRELATION OF VISCOSE COMPONENTS

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The effect of various components of viscose on its properties, such as viscosity, ripeness, etc., has been noted in a series of papers. The optimal concentrations of alkali in viscose for least viscosity and ripeness were reported in articles by Westhoff [1] (8-9% NaOH), Heuser and Schuster [2] (8 vol.% NaOH), Lieser [3] (7% NaOH) and Rassow and Aehnelt [4] (9% NaOH). The effect of alkali concentration on viscosity and ripeness of viscose were examined by S. M. Liepatoff [5] and Mukoyama [6]. Trithiocarbonate and sodium carbonate increase [2], while sodium sulfide decreases the viscosity of viscose [7]. We previously reported new data on the effect of sodium hydrosulfide, sodium thiosulfate, sodium disulfide and other polysulfide compounds on viscose [8].

In the experiments described below we examined the effect of the concentration of sodium hydroxide and some other salt components of viscose (Na_2S, Na_2CS_3, Na_2CO_3, Na_2SO_3, $Na_2S_2O_3$) in aqueous and alkaline solutions on the decomposition rate of cellulose xanthogenates. The decomposition rate of purified cellulose xanthogenate under the effect of water and aqueous electrolyte solutions and also the changes in viscose composition during ripening were investigated. Various chemical methods and potentiometric titrations were used to establish the conversions of cellulose xanthogenate and the sulfur-containing products formed.

Experiments on xanthogenate decomposition in pure water showed that on storing the solutions, on the very first day there was partial evolution of free carbon disulfide, which was not converted into trithiocarbonate due to the absence of sodium sulfide and alkali in the solution. Even in solutions of xanthogenate in sodium hydroxide, there was evolution of carbon disulfide. However, solutions of xanthogenate in sodium sulfide contained no free carbon disulfide as under these conditions trithiocarbonate formed rapidly. Solutions of xanthogenate in sodium sulfide were characterized by a bright orange color. Thus, the cellulose xanthogenate reactions include not only hydrolytic elimination of dithiocarbonate groups to form sodium dithiocarbonate or simply desulfuration of them to give acid carbonate esters of cellulose (this has not been confirmed up to now) with the composition $[C_6H_{10-x}O_{5-x}(OCOONa)x]_n$, but also involve the evolution of free carbon disulfide due to decomposition of the dithiocarbonate groups.

Cellulose xanthogenate decomposed quite rapidly in aqueous solutions and in neutral salt solutions, for example in thiosulfate, but an increase in alkalinity of the solution slowed down its decomposition. Substances with an acid reaction accelerate the decrease in the degree of xanthogenation but bicarbonate hardly affects xanthogenate decomposition.

Sodium trithiocarbonate has been considered as a destabilizer and sodium hydrosulfide as a stabilizer of viscose. It was found that in the first "ripening" stages, xanthogenate was more stable in sodium trithiocarbonate solutions, due to the higher pH of this salt. Xanthogenate decomposed in a sodium trithiocarbonate solution at a constant rate, while in a sodium hydrosulfide solution the rate decreased toward the end of ripening so that at the moment of coagulation the degree of xanthogenation in a sulfite solution was higher. This was due to the fact that the sodium sulfite [8] participated in the sulfur rearrangement (with the polysulfide materials), and, besides that, it was an anti-oxidant, as shown by the accumulation of reaction products from the xanthogenate groups in the solution.

Xanthogenate decomposition slowed down in a soda solution and in a sodium hydroxide medium. If electrolytes were added to the alkaline solutions of xanthogenate and not pure water, the various additives hardly affected the decomposition of xanthogenate as the high value of the solution's pH was the deciding factor.

The medium in which the xanthogenate is ripened greatly affects the coagulation of the solutions. Thus in the presence of sodium hydrosulfite and sodium sulfite, xanthogenate solutions were readily coagulated at relatively high degrees of xanthogenate esterification. Coagulation of viscose, containing salts, was investigated by N. V. Mikhailov, V. N. Maiboroda and V. A. Kargin [9], who considered this process as resulting from a decrease in xanthogenate solubility. Our experiments with aqueous solutions of pure xanthogenate showed the essential role of the anions of the salts. The deciding factor in the coagulation of alkaline solutions of cellulose xanthogenate is the sodium hydroxide content of the solution.

An analysis of xanthogenate solutions showed that the main titratable product of cellulose xanthogenate decomposition in alkali and in pure aqueous or aqueous salt solutions was sodium sulfide and the maximum amount of it accumulated in sodium hydroxide solutions (especially at 1% concentration). Sodium trithiocarbonate was detected later than sodium sulfide in the "ripening" of cellulose xanthogenate solutions. Apparently, it formed as the carbon disulfide evolved was bound by the sodium sulfide. The only exceptions were xanthogenate solutions in sodium sulfide, in which trithiocarbonate may be detected at the very beginning of the chemical reaction.

Investigation of the changes in viscose composition during ripening showed that in viscose, as in purified xanthogenate solutions, sodium sulfide formed before trithiocarbonate. Very young viscoses contained more sodium sulfide than trithiocarbonate. Then sodium sulfide content decreased as the dithiocarbonate groups split off from the cellulose and the amount of trithiocarbonate greatly increased. However, if the viscose was diluted with water during ripening there was a rapid increase in the amount of sodium sulfide and a slower increase in the amount of trithiocarbonate, due to the hydrolysis of the latter.

Sodium sulfide should be considered as an intermediate stage in trithiocarbonate formation, but trithiocarbonate, in its turn, is hydrolyzed to sodium sulfide and sodium hydrosulfide, and the latter may be oxidized to give polysulfide materials [1].

The problem of the changes in the sodium hydroxide content of viscose during its ripening seemed interesting. It was assumed [4, 11] that sodium hydroxide is chemically bound (as in molecular compounds) or adsorbed by xanthogenate and some sulfide compounds, which are titrated together with sodium hydroxide by silver nitrate. As the viscose ripened and the dithiocarbonate groups were eliminated from cellulose xanthogenate, the adsorbed sodium hydroxide remained in the cellulose and probably at a concentration somewhat greater than that in the viscose itself.

Experiments showed that the amount of sodium hydroxide in the viscose changed little during the ripening and remained, one could say, constant within the limits of the error of the analysis, which, as a matter of fact, requires further development. As the sulfur content of viscose varied between 2-5% and the amount of sodium in the sulfide compounds was consequently small, there was always a large excess of free sodium hydroxide as compared with the number of molecules used in the conversion of the sulfur-containing substances.

The problem of how the amount of dithiocarbonate groups gradually decreases in cellulose xanthogenate as the viscose ripens has been discussed for a number of decades. Two main viewpoints have been expressed: 1) carbon disulfide and sodium hydroxide are eliminated and the carbon disulfide then reacts with the cellulose and sodium hydroxide, due to which the degree of xanthogenation decreases and the amount of sulfur-containing side products increases, as is shown graphically in Geiger's scheme [12]; 2) it is due to the hydrolytic elimination of sodium dithiocarbonate, according to Parry [13, 8]. In fact, both modes of xanthogenate conversion exist but one of them predominates, depending on the conditions and mainly on the alkalinity of the medium and the temperature. A decrease in alkalinity and an increase in temperature promotes carbon disulfide evolution, while an increase in alkalinity, stabilizing the xanthogenate, causes hydrolysis and the elimination of the dithiocarbonate groups.

EXPERIMENTAL

1. Analysis methods. For investigating the effect of sodium hydroxide in various concentrations on the conversions of cellulose xanthogenate in comparison with its conversions in pure water, we used freshly prepared samples of purified xanthogenate (precipitated from previously neutralized viscose with ethyl alcohol). From these samples we prepared equal concentration solutions in water and various concentrations of alkali. As the solutions ripened, aliquot samples were taken and their contents of undecomposed xanthogenate ("xanthogenate sulfur") and decomposition products ("side product sulfur") determined.

For the determinations we used potentiometric titration with silver nitrate, using a silver electrode, and the usual iodometric titration (Geiger's method). In some experiments we also used the dixanthogenide method: the xanthogenate was isolated from the solution as the dixanthogenide (treatment with iodine) and then the sulfur content determined by bromide – bromate oxidation.

It was first established that successful application of the iodometric method to solutions of various alkalinities required that the titration be performed in an acetic acid medium with a quite definite excess of acid over the alkali in the solution, namely 7-8 times. Approximately this ratio was also used in Geiger's usual method. Titration was also possible in a hydrochloric acid medium with any slight excess of acid. Additional testing of the potentiometric method on model solutions, whose results we give briefly here, showed that satisfactory data was only obtained in the determination of sodium sulfide. It was necessary, however, to bear in mind the fact that in the presence of disulfide, the latter was determined together with the sodium sulfide, so that in alkaline solutions we obtained somewhat high results since the disulfide was titrated with silver nitrate together with a certain amount of alkali (1 mole of disulfide combines with up to 2 moles of sodium hydroxide in a titration in an alkaline medium). The alkalinity of the medium did not affect the accuracy of sulfide determination. Since the amount of polysulfide compounds in the viscose was not usually large, the potentiometric titration with silver nitrate may be considered suitable for the determination of sodium sulfide due to the lack of more accurate methods. The potentiometric method was least suitable for the determination of xanthogenate. We obtained indefinitely high results due to titration of the xanthogenate and part of the alkali by the silver nitrate. The trithiocarbonate may only be determined together with perthiocarbonate. Also in this case we obtained high results due to the combination of both salts with alkali. Here, however, the ratio was more definite than in the case of xanthogenate: for each salt, about 2 moles of sodium hydroxide combined with 1 mole of salt. Thus, with a sufficient amount of alkali in the solution, the results of the determination were high by approximately 2 times, which made it possible to use the potentiometric method for comparative determinations of trithiocarbonate (together with perthiocarbonate) in solutions of sufficiently high alkalinity. To eliminate the effect of alkali in the results of potentiometric determinations, preliminary neutralization of the viscose with acetic acid was proposed [14]. But, as we discovered, this gave less distinct titration curves, which lead to significant errors in the determinations. Considering what has been said, we used the potentiometric method only for the determination of sodium sulfide (considering that the disulfide content was insignificant under the given conditions) and for the qualitative detection of trithiocarbonate (together with perthiocarbonate) in the experiments described

To examine the decomposition of xanthogenate in salt solutions, it was necessary to determine xanthogenate in the presence of the particular salts. The usual methods, for example iodometric titration, were unsuitable for these determinations. In this series of experiments, we isolated the xanthogenate from the solution as the insoluble zinc salt, which was then assayed for sulfur content.* As is known, the reaction between sodium xanthogenate and a zinc salt in dilute solutions does not go to completion [3, 15]. However, as we showed in experiments with xanthogenate samples and also with viscose, by performing this reaction in the presence of sodium acetate or sodium sulfate, it is possible to use it to follow the decomposition of xanthogenate. The data obtained were 7-8% lower in absolute value than the results obtained by other methods. However, they gave a similar comparative picture of the changes (Fig. 1).

The determination procedure, using the "zinc" method, was reduced to the following. A sample of the xanthogenate solution under examination was taken at a given stage of ripeness and after decomposition of the

* As subsequent experiments showed, a convenient method of determining xanthogenate for such investigations was based on its separation from the mineral salt components with adsorbents (for example charcoal).

side sulfide products with acetic acid, a concentrated solution of sodium acetate was added followed by excess of a concentrated zinc sulfate solution. After 5-10 minutes, the zinc xanthogenate precipitate was filtered off, triturated in a mortar with aqueous alcohol, alcohol and ether and analyzed for sulfur content by decomposition with mineral acid and determination of the carbon disulfide liberated as potassium ethylxanthogenate.

To characterize the viscose at various stages of ripeness, we determined the sodium hydroxide, sodium sulfide and trithiocarbonate contents and the decrease in degree of xanthogenation of the cellulose. In choosing the methods of analysis, we were guided by their suitability, even for comparative determinations. We determined the degree of xanthogenation by iodometric titration, the sodium sulfide by potentiometric titration with silver nitrate and the trithiocarbonate content was expressed approximately as the difference between the consumption of iodine in the titration of the viscose in a hydrochloric acid medium and the consumption of silver nitrate in the determination of sodium sulfide. With a sufficient absolute trithiocarbonate content of the viscose, this determination must have recorded at least substantial changes in the amount of trithiocarbonate as the solution ripened.

Recently, the sodium hydroxide content of viscose has been determined by titrating the viscose with acetic acid [16] or bicarbonate [17] with a glass electrode. As a result of a thorough examination of the two titrations on model solutions; we chose the bicarbonate method, but modified it in comparison with the procedure proposed by the authors. The changes were: 1) inclusion of a correction for the sodium sulfide content of the viscose, as it was found that together with the sodium hydroxide, the bicarbonate also titrated the sodium sulfide to hydrosulfide, i.e., the total NaOH + 1/2 Na_2S was determined; 2) the viscose was titrated directly and not the liquid obtained after centrifuging the precipitated xanthogenate as the latter inevitably results in the loss of some unconditionally variable amounts of sodium hydroxide, carried down from the solution by the xanthogenate.

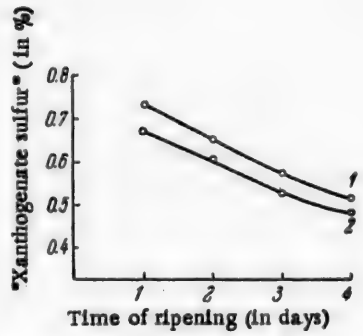

Fig. 1. Changes in the "xanthogenate sulfur" content during the ripening of viscose. 1) By the iodometric method; 2) by the zinc method.

We should note that with the bicarbonate and also the acetic acid, we titrated all the chemically unbound sodium hydroxide, which also included that which may have been additively bound to the xanthogenate and the tri- and perthiocarbonates. This was readily shown by titrations of appropriate model solutions. The accuracy of the bicarbonate method, which was 2-3% in work with model solutions, fell on application to viscose, due to the need for corrections for the sodium sulfide content, which was determined approximately for viscose, as noted above.

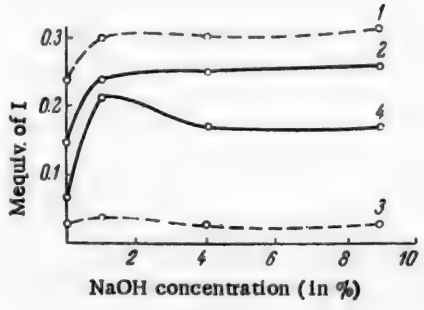

Fig. 2. Decomposition of xanthogenate in alkali at various concentrations. Sample I (composed of 20 ml of 1.5% xanthogenate solution, in mequiv. of iodine): 1) "Xanthogenate sulfur" after 1 hour; 2) the same after 1 day; 3) "side product sulfur" after 1 hour; 4) the same after 1 day.

2. The effect of sodium hydroxide concentration on xanthogenate decomposition. The data obtained, illustrated in Figs. 2-4, show that xanthogenate decomposes more slowly in alkaline solutions than in aqueous solution, but the concentration of alkali (in the range 1-10%) hardly affects the rate of decomposition of the xanthogenate. Determinations by the iodometric and xanthogenide methods gave identical results. As is known, Geiger came to the same conclusion in his time during the investigation of viscoses of different alkalinities [12]. However, the concentration of alkali substantially affects the coagulating capacity of xanthogenate solutions. Thus, for example, 1-2% solutions of xanthogenate in 1-2% sodium hydroxide coagulated after several days, but in 8-10% alkali, this occurred only after 1-2 months.

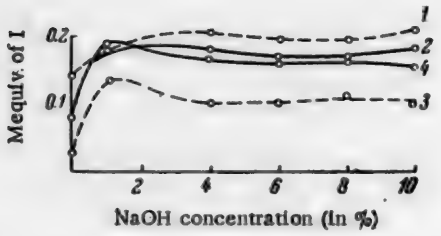

Fig. 3. Decomposition of xanthogenate in alkali at various concentrations. Sample II (composed of 20 ml of 1% xanthogenate solution, in mequiv. of iodine). 1) "Xanthogenate sulfur" after 1 day; 2) the same after 2 days; 3) "side product sulfur" after 1 day, 4) the same after 2 days.

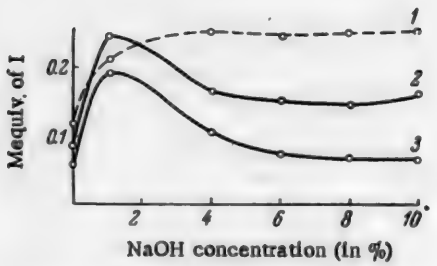

Fig. 4. Decomposition of xanthogenate in alkali at various concentrations. Sample III (composed of 20 ml of xanthogenate solution in mequiv. of iodine for 3 days ripening). 1) "Xanthogenate sulfur"; 2) "side product sulfur"; 3) sodium sulfide.

The concentration of alkali apparently has some effect on the composition of the xanthogenate decomposition products. According to potentiometric determinations, considerable amounts of sodium sulfide are formed during the ripening of alkaline xanthogenate solutions and under the given conditions, sodium sulfide is the main decomposition product of xanthogenate.

The maximal amounts of sodium sulfide were observed in solutions with 1% alkali. Even after 2-3 days ripening, about 25% of the original xanthogenate sulfur in these solutions was bound in the form of sulfide. In solutions with higher alkali concentrations, the sulfide content was approximately half the value and depended little on the alkali concentration. Consequently, the maximal amounts of decomposition products, titratable with iodine, were also formed in 1% alkali solutions. A parallel investigation of the sodium sulfide in alkaline solutions with various sodium hydroxide contents showed a slightly slower rate of conversion of the sulfide in 1% sodium hydroxide in comparison with solutions of it in stronger alkali (the numerical data is not given).

As was to be expected, according to the potentiometric titration curves, the trithiocarbonate content of the solutions investigated was very small. Generally it was impossible to detect trithiocarbonate in 0.5% xanthogenate solution with alkali concentrations below 6%. In 6% alkali solution, only traces of trithiocarbonate was found. With higher xanthogenate concentrations, it was possible to detect trithiocarbonate at any alkali concentration, but only after storing the solution for a definite time, sometimes only after 2 days. The low concentration and the later appearance of trithiocarbonate in comparison with sodium sulfide indicates that the formation of sulfide precedes the formation of trithiocarbonate in the decomposition of xanthogenate. However, it is necessary to take into account the possibility of the secondary formation of sodium sulfide due to hydrolysis of the trithiocarbonate, especially in highly dilute solutions as in the experiments described. Below it is shown that sodium sulfide in viscose also arises as a result of trithiocarbonate decomposition, together with the primary formation as a result of xanthogenate decomposition.

Aqueous solutions of xanthogenate differ from alkaline solutions not only in the higher degree of xanthogenate decomposition but also in the considerably lower content of decomposition products titratable with iodine and silver nitrate. This is due to the lack of cation (sodium) in this case and, apparently, to a different course of xanthogenate decomposition in an aqueous solution in comparison with alkaline solutions. Apparently, the decomposition of xanthogenate in an aqueous solution mainly proceeds with the elimination of free carbon disulfide. However, we should note that we also observed the evolution of free carbon disulfide during the ripening of alkaline solutions of xanthogenate (confirmed by a triethylphosphine test). It is characteristic that in aqueous solutions of xanthogenate also the main titratable decomposition product is sodium sulfide.

3. The effect of some components of viscose on xanthogenate decomposition. The effect of the salt components of viscose (Na_2S, Na_2CO_3, Na_2SO_3, Na_2CS_3, $Na_2S_2O_3$) on xanthogenate decomposition in aqueous and alkaline solutions was examined. For the investigation we used the same sample of purified xanthogenate

as in the previous experiments. So that the xanthogenate would be in contact with the given additive from the very beginning of its ripening, it was dissolved directly in an aqueous or aqueous-alkaline solution of the appropriate salt. The additives were added in equimolecular ratios, amounting to about 2 moles per mole of xanthogenate dithiocarbonate group. The data obtained, which is presented in Figs. 5-8 and the Table, shows that the chemical stability of the xanthogenate solutions is determined mainly by the alkalinity of the solution. This follows not only from comparison of the data on xanthogenate decomposition in aqueous and alkaline solutions, but also from an investigation of the ripening of aqueous salt solutions (Figs. 5-8 on the Table). Here the dependence of the rate of xanthogenate decomposition on the pH of the solution is very clear, especially during the first days of ripening, when the solution still contains small amounts of decomposition products, whose presence, and also the possibility of whose reaction with the added salts may affect further decomposition of the xanthogenate. In salt solutions with low pH ($Na_2S_2O_3$, Na_2SO_3), during the first days xanthogenate decomposition proceeds approximately at the same rate as in an aqueous solution. In solutions with higher pH (Na_2S, Na_2CO_3, Na_2CS_3), the decomposition proceeds more slowly. The data thus obtained are close to data for the decomposition of xanthogenate in a sodium hydroxide solution of equivalent concentration. Further on the picture changes: the nature of the additives begins to have an effect. While the curve of xanthogenate decomposition in a thiosulfate solution remains close to the curve of xanthogenate decomposition in an aqueous solution to the end of ripening, in a sulfite solution there is a retardation of xanthogenate decomposition (in the second period of ripening, the curve for a sulfite solution is flatter). It is possible that this is just due to the fact that there are already considerable amounts of decomposition products in the solution at this time and the reaction of sulfite with these [8] also controls its retarding effect on the ageing of viscose. A different course of the xanthogenate decomposition curves was observed on adding sodium trithiocarbonate and sulfide. While at the beginning of ripening (first days) xanthogenate decomposition in these solutions is slowed by the high pH of the solution, further on it continues at almost the same rate, which exceeds the rate of xanthogenate decomposition at this stage of ripening in solutions of the rest of the salts.

The Effect of Adding Bicarbonate and Soda on the Ripening of Aqueous Solutions of Xanthogenate

Expt. No.	Additive	Amount of additive		"Xanthogenate sulfur" content of 20 ml of solution (in mequiv.)	
		in moles per CSSNa	percentage content of solution	time of ripening (in hours)	
				24	70
1	H_2O	—	—	0.74	0.38
	NaOH	3.3	0.32	1.14	0.50
	Na_2CO_3	1.7	0.42	1.04	0.58
	$NaHCO_3$	1.7	0.34	—	0.36
				15	40
2	H_2O	—	—	—	0.60
	NaOH	2.8	1.34	1.34	1.14
	Na_2CO_3	1.4	1.24	1.24	1.06
	$NaHCO_3$	1.4	1.22	1.22	0.84

At the end of ripening (after 3 days), the xanthogenate in solutions with sulfide and trithiocarbonate added shows only slightly less decomposition than in an aqueous solution. The constancy of the xanthogenate decomposition rate in these solutions during this period of ripening, when the solution already contains and continues to accumulate xanthogenate decomposition products, indicates that the effect of these additives on the course of xanthogenate decomposition does not depend on the presence of side products in the solution.

The effect of the alkalinity of the solution on its chemical stability is shown most clearly by the aqueous soda solution (Table). Xanthogenate decomposition in a soda solution proceeds considerably more slowly than in the other aqueous salt solutions. The data for aqueous soda solutions during all the ripening are close to the data for solutions of xanthogenate in sodium hydroxide of equivalent concentration. In this case, the nature of the anion evidently does not affect the course of xanthogenate decomposition. However, these soda solutions and also to a somewhat lesser extent, solutions of xanthogenate in sodium sulfide, had the lowest colloidal

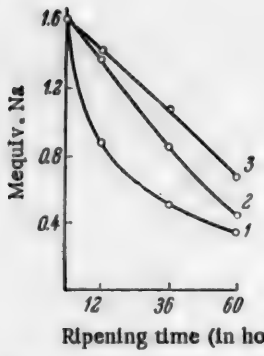

Fig. 5. The effect of sodium sulfide on xanthogenate decomposition. 1) Aqueous solution of xanthogenate; 2) solution with sodium sulfide added; 3) solution with sodium hydroxide added.

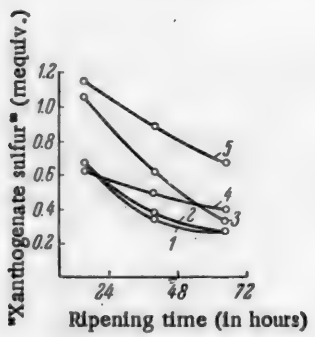

Fig. 6. The effect of adding salts on xanthogenate decomposition in aqueous solution. 1) Aqueous solution of xanthogenate; 2) solution with sodium thiosulfate added; 3) solution with sodium thiocarbonate added; 4) solution with sodium sulfite added; 5) solution with sodium hydroxide added.

stability. They coagulated earlier than the rest and at a higher degree of xanthogenate substitution. In rate of coagulation, the soda solutions are close to xanthogenate solutions with bicarbonate added. However, in the latter, the xanthogenate is decomposed considerably more rapidly, for example at the same rate as in aqueous or thiosulfate solutions. In their turn, the bicarbonate solutions coagulate earlier than aqueous and thiosulfate solutions. This indicated that the chemical stability does not determine the colloidal chemical stability of aqueous soda solutions and that the latter is controlled to a known extent by the effect of the anion of the added salt. It is impossible to explain otherwise the earlier coagulation of soda and sulfide solutions in comparison with other aqueous salt solutions and also the similar coagulation capacity of soda and bicarbonate solutions. The higher degree of xanthogenate substitution at coagulation of these solutions is probably caused by the retardation of the chemical processes during the growth of a form of structure in the solution.

The role of alkali as the main factor in the stability of xanthogenate solutions shows most clearly in those experiments in which we studied the effect of adding salts not to aqueous, but to alkaline solutions of xanthogenate (Figs. 7 and 8). Even with comparatively small concentrations of sodium hydroxide (1 mole per xanthogenate dithiocarbonate group or 0.2% in solution) the presence of added salts in the solution hardly affects the rate of xanthogenate decomposition or the coagulation capacity of the solutions. Only for solutions with soda added did we observe some retardation of xanthogenate decomposition at the beginning of ripening in comparison with solutions of pure alkali of equal concentration (allowing for the extra increase in alkalinity) and on increasing the soda content to 1%, coagulation of the solution occurred earlier. On the other hand, comparatively small changes in the alkalinity of the solution (at the concentrations below 1%) considerably affected the ripening of the solution. Thus increasing the alkali content from 1 to 2 moles per dithiocarbonate group (from 0.2 to 0.4% in the solution) substantially retarded xanthogenate decomposition. The colloidal stability was also correspondingly increased; solutions with 0.2% sodium hydroxide coagulated 1-2 days earlier than solutions with 0.4% alkali.

The absence of a direct effect of added salts on the rate of xanthogenate decomposition, which follows from our experiments, does not exclude the possibility of their indirectly affecting the course of ripening by interaction with the side products and as a result of this, shifting the equilibrium of the reactions which determine the ripening of xanthogenate solutions. It is obvious that in technical viscoses such an effect must be more noticeable than in solutions of purified xanthogenate and this is actually shown by sulfate, for example. The retarding effect of sulfate on the ripening of viscose has long been known and we observed this to a small extent in a solution of pure xanthogenate, which began to ripen in the complete absence of side products. Some external indications, for example, the different color of the xanthogenate solutions with different additives, however, indicated that certain changes were possible in the composition of solutions of purified

xanthogenate under the effect of added salts. Thus, bicarbonate solutions differed from the rest in their bluish green color, sulfite solutions were grey, thiosulfate and aqueous solutions green, alkaline and many of the alkaline salt solutions yellow-green and sulfide solutions bright orange. The appearance of an orange color immediately after solution of the xanthogenate in sulfide solution indicated the formation of trithiocarbonate in it right from the very beginning and this was confirmed potentiometrically. In sulfide solutions, in contrast to the others, free carbon disulfide was not once found during the whole course of the ripening and this confirms the high rate of reaction of carbon disulfide with sodium sulfide, which is apparently the main method of trithiocarbonate formation in xanthogenate decomposition.

However, over the range of our experiments, there were no noticeable changes in the composition of the main xanthogenate decomposition products under the effect of the additives introduced. The main titratable xanthogenate decomposition product in aqueous salt solutions and in aqueous and alkaline solutions was sodium sulfide. The sodium sulfide contents of solutions with additions of sulfite, thiosulfate and carbonate were close to those of pure aqueous solutions of xanthogenate, but the ripening time was a factor of $2\frac{1}{2} - 3$ less than in solutions with equivalent additions of sodium hydroxide. No substantial difference was observed in the sodium sulfide contents of solutions with the given additives, though, as a rule, solutions with sulfite added contained slightly more sodium sulfide than thiosulfate and soda solutions. At the moment of coagulation of the solutions (after 3-4 days), about 15% of the original xanthogenate sulfur was in the form of sulfide in alkaline solutions and about 4-5% in aqueous and aqueous salt solutions.

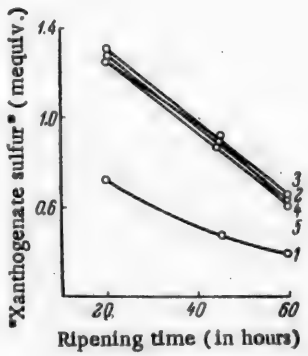

Fig. 7. Effect of adding salts on xanthogenate decomposition in an alkaline solution. 1) Aqueous solution of xanthogenate; 2) alkaline solution of xanthogenate; 3) alkaline solution with sodium trithiocarbonate added; 4) alkaline solution with sodium thiosulfate added; 5) alkaline solution with sodium sulfite added.

Trithiocarbonate could not be determined quantitatively in these experiments. We were obliged to limit ourselves to the qualitative data of potentiometric titration. According to these results, trithiocarbonate appeared in all the solutions examined, except sulfide solutions, later than sodium sulfide, usually only after 2 days ripening. In one of the experiments, in which xanthogenate with a low degree of substitution (γ = 25) was used, trithiocarbonate was detected only after 4 days ripening. Due to the very small values of the steps on the potentiometric titration curves in the region of trithiocarbonate separation, it was impossible to distinguish substantial differences in the trithiocarbonate contents of solutions with various additives, but it was possible to observe some increase in the trithiocarbonate content of solutions as they ripened.

4. Changes in the composition of viscose during ripening. Experiments (Fig. 9) showed that in normal viscose, as in the solutions of pure xanthogenate examined above, the formation of sodium sulfide preceded the formation of trithiocarbonate. In young viscoses, there is more sodium sulfide than trithiocarbonate. Then, as the viscose ages, the ratio changes: the trithiocarbonate content increases and the sulfide continuously decreases. Thus, sodium sulfide is undoubtedly an intermediate stage in the formation of trithiocarbonate. But the reverse process also occurs with the formation of sodium sulfide from decomposition of trithiocarbonate. This is shown particularly graphically by observations on the ripening of dilute viscose. Figure 10 illustrates the results of determining the trithiocarbonate and sulfide in viscose, diluted 10 times with distilled water on the second day of ripening. During the ripening of dilute viscose, there is, on the contrary, an accumulation of sodium sulfide, due to an increase in the rate of trithiocarbonate decomposition at the high dilution. The trithiocarbonate content of dilute viscose increases correspondingly more slowly than in normal viscose and even decreases slightly immediately after dilution. The dilution of the viscose in the experiment described approximately corresponded to the concentration of the solutions of pure xanthogenate examined above.

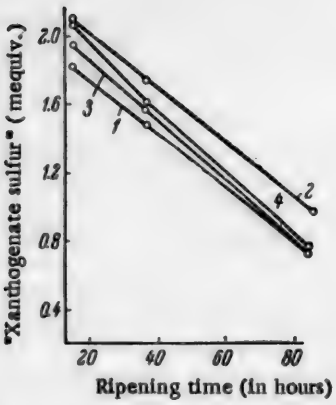

Fig. 8. Effect of sodium carbonate on xanthogenate decomposition in alkaline solution. 1) Solution of xanthogenate in 0.2% sodium hydroxide, 2) solution of xanthogenate in 0.4% sodium hydroxide, 3) solution of xanthogenate in 0.2% sodium hydroxide with 1 equiv. of sodium carbonate added, 4) the same with 2 equiv. of sodium carbonate added.

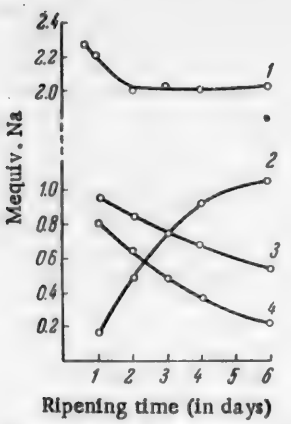

Fig. 9. Changes in the composition of viscose during ripening (in mequiv. of sodium per 2 g of viscose) 1) Sodium hydroxide; 2) trithiocarbonate; 3) xanthogenate; 4) sulfide.

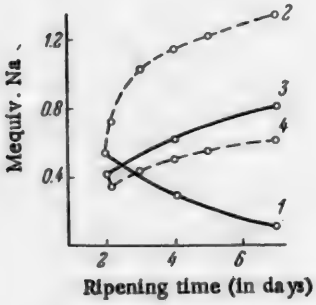

Fig. 10. The effect of dilution on the formation of sodium sulfide and sodium trithiocarbonate in viscose (viscose diluted on second day). 1) Sodium sulfide content of normal viscose; 2) the same of dilute viscose; 3) sodium trithiocarbonate content of normal viscose; 4) the same of dilute viscose.

The presence of only very small amounts of trithiocarbonate in the latter was consequently partly responsible for the ease of decomposition of trithiocarbonate at the high dilutions. As we observed, the sodium hydroxide content remained practically constant during the whole course of the ripening, apart from the first 1-2 days, when there was a little consumption of sodium hydroxide (about 10%) due to additional side reactions during the solution of the xanthogenate.

SUMMARY

1. Cellulose xanthogenate decomposes more rapidly in aqueous rather than in alkaline solutions and as the alkalinity of the xanthogenate solutions increases, their stability to coagulation likewise increases.

2. The rate of xanthogenate decomposition in salt solutions with low pH is similiar to the rate of xanthogenate decomposition in water. As the pH of the salt solutions is raised the xanthogenate decomposition slows down. The addition of sodium hydroxide to salt solutions of xanthogenate retards its decomposition, as in pure alkali solutions. The nature of the salt additives has a definite effect on the coagulation of aqueous salt xanthogenate solution. Sodium hydrosulfide has a particular effect on xanthogenate decomposition as it retards its ripening by reactions with the decomposition products.

3. During cellulose xanthogenate decomposition in aqueous or aqueous electrolyte solutions and in ordinary viscose, large amounts of sodium sulfide are formed as a primary product which by reacting with carbon disulfide forms trithiocarbonate, although it, itself, may be formed by the hydrolysis of trithiocarbonate.

4. The sodium sulfide contents decrease and those of trithiocarbonate increase as pure xanthogenate solutions and viscose ripen.

5. The sodium hydroxide content of viscose remains almost constant during the whole ripening process, except fo the first 1-2 days, when it decreases somewhat.

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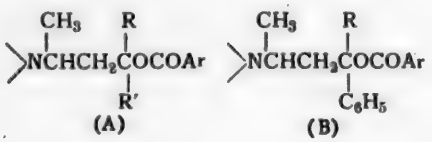
SYNTHETIC ANESTHETICS

XVII. ESTERS OF 3-DIALKYLAMINO-2-METHYL-1,1-DIALKYLPROPAN-1-OLS

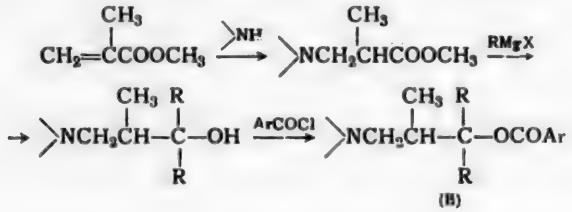
I. N. Nazarov* and L. Z. Kazaryan

Previous papers from our laboratory [1, 2] described the synthesis of esters of tertiary γ-amino alcohols of the following structure:



(A) (B)

In order to investigate systematically the relation of the physiological activity of this type of compound to the structure, in particular to the character of the alcohol radicals (R) and position of the methyl group in the aminopropane chain, we also synthesized a series of esters, represented by formula (B), which were prepared from methyl methacrylate by the following scheme:



(B)

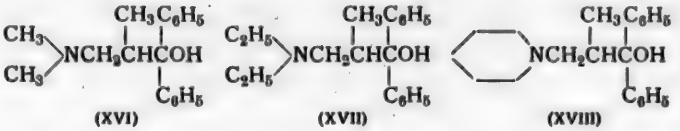
Methyl methacrylate added dimethylamine, diethylamine and piperidine [3] smoothly at room temperature to give over 90% yields of the corresponding amino esters. The amino ester yield depended to a large extent on the duration of standing of the mixture of the particular secondary amine and methyl methacrylate. Thus, for example, equimolecular amounts of piperidine and methyl methacrylate reacted at the following rate:

Duration of standing at room temperature (in days)	1	2	3	12
Amino ester yield (in %)	54	82	94	98.5

Reaction of the esters of β-dimethylamino- and β-diethylaminoisobutyric acids obtained by this method with methylmagnesium iodide and with ethyl-, propyl-, butyl- and isoamylmagnesium bromides gave the corresponding tertiary amino alcohols (I–X), given in Table 1, and in some cases intermediate reaction products, β-amino ketones (XI–XV) given in Table 2, were also isolated.

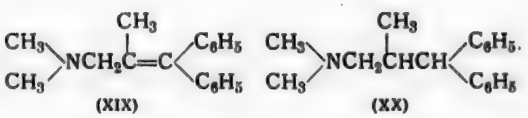
*Deceased.

Treatment of methyl esters of β-dimethylamino-, β-diethylamino- and β-piperidinoisobutyric acids with phenylmagnesium bromide gave tertiary aliphatic-aromatic amino alcohols (XVI, XVII and XVIII).



(XVI) (XVII) (XVIII)

These alcohols were also prepared by reacting a Grignard reagent with appropriate amino ketones, which were obtained, in their turn, from propiophenone by the Mannich reaction [4]. All attempts at esterification of alcohols (XVI, XVII and XVIII) lead only to the formation of their dehydration products. Thus, heating 3-dimethylamino-2-methyl-1,1-diphenylpropanol-1 (XVI) with benzoyl chloride and acid chlorides of other acids gave 3-dimethylamino-2-methyl-1,1-diphenylpropene (XIX), which was also prepared by dehydrating this alcohol with a mixture of hydrochloric and acetic acids. Hydrogenation of the unsaturated amine (XIX) gave 3-dimethylamino-2-methyl-1,1-diphenylpropane (XX).



(XIX) (XX)

Esterification of alcohols (I–V) with benzoyl chloride and p-nitrobenzoyl chloride gave the corresponding benzoates (XXI–XXV) and p-nitrobenzoates (XXVI–XXX). The latter were reduced with hydrogen in the presence of a nickel catalyst of p-aminobenzoates (XXXI–XXXIII). All the esters listed were prepared in the form of hydrochlorides or oxalates that crystallized well.

Esterification of alcohols (VI–X) gave benzoates, p-nitrobenzoates and p-aminobenzoates (XXXIV–XL). However, most of them did not give salts that crystallized (hydrochlorides and oxalates) and the products were characterized as the free bases. We had also observed previously that compounds containing a diethylamino group often did not give crystalline hydrochlorides. All the esters prepared in this work are given in Table 3.

Pharmacological tests* showed that the hydrochlorides of benzoates (XXI and XXII) were 3 times more active than novocaine. The benzoates (XXIV and XXV) were prepared and tested in the form of oxalates and it is possible that due to this they were found to be of low activity. The introduction of an amino group into the benzoic acid radical decreased the anesthetic activity of these compounds. Thus, the activity of the hydrochloride of the p-aminobenzoate (XXXI) was equal to that of novocaine (cf. with ester XXI), while its oxalate had almost no activity. Benzoate (XXXIV) and p-aminobenzoate (XL), tested in the form of oxalates, had no anesthetic activity.

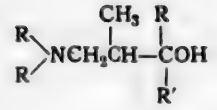
EXPERIMENTAL

Esters of β-dialkylaminoisobutyric acids [3]. Esters of β-dialkylaminoisobutyric acids were prepared by the addition of secondary amines (dimethylamine, diethylamine, piperidine) to methyl methacrylate. As an example, we describe the preparation of methyl β-dimethylaminoisobutyrate below. 68 g of gaseous dimethylamine, dried over solid potassium hydroxide, was passed over a period of 1 hour into a solution of 100 g of freshly distilled methyl methacrylate in 50 ml of methanol. The mixture was kept at room temperature for 3 days and then distilled in vacuum. We obtained 140.6 g (93%) of methyl β-dimethylaminoisobutyrate.

B. p. 70-71° (24 mm), n_D^{20} 1.4201, d_4^{20} 0.9116, MR 40.14; calc. 40.00.

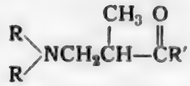
* The pharmacological tests were carried out in the pharmacological laboratories of the S. Ordzhonikidze All-Soviet Sci. Res. Inst. of Chem. and Pharm., under the direction of Prof. Mashkovsky.

TABLE 1

Tertiary alcohols 

No. of sample	R	R′	Boiling point at given pressure (mm)	n_D^{22}	d_4^{22}	MR_D		Yield (in %)	Nitrogen content (in %)	
						calc.	found		calc.	found
I	CH_3	CH_3	59—60° (10)	1.4285	0.8394	44.63	44.60	73.2	9.55	9.79. 9.98
II	CH_3	C_2H_5	51—51.5 (2)	1.4437	0.853	53.84	53.84	82.9	8.09	8.28. 8.47
III	CH_3	C_3H_7	63—64 (1)	1.4425	0.841	63.06	63.08	88.5	7.97	7.12. 7.29
IV	CH_3	C_4H_9	83—84 (2)	1.4465	0.8454	72.30	72.32	70.5	6.11	6.11. 6.00
V	CH_3	Iso-C_5H_{11}	97—98 (1)	1.4490	0.8474	81.46	81.55	56.2	5.45	5.77. 5.90
VI	C_2H_5	CH_3	70—71 (6)	1.4405	0.8465	53.91	53.84	57.9	8.08	8.02. 8.37
VII	C_2H_5	C_2H_5	87—88 (5)	1.4367	0.834	62.97	63.08	47.8	6.97	7.05. 7.14
VIII	C_2H_5	C_3H_7	75—76 (2)	1.4335	0.827	72.05	72.05	33.2	6.11	6.13. 6.37
IX	C_2H_5	C_4H_9	93—91 (2.5)	1.4405	0.833	81.39	81.55	36.1	5.45	5.50. 5.66
X	C_2H_5	Iso-C_5H_{11}	135—135.5(3.5)	1.4503	0.843	90.91	90.79	58.1	4.91	4.83. 5.35

TABLE 2

β-Aminoketones 

No. of sample	R	R′	Boiling point at given pressure (mm)	n_D^{22}	Yield (%)	Nitrogen content (in %)		Melting point of 2,4-dinitrophenylhydrazone
						calc.	found	
XI	CH_3	C_4H_9	60—63° (2)		10	8.18	8.03, 8.05	—
XII	CH_3	Iso-C_5H_{11}	63—64 (1)	1.4315	28	7.58	7.41, 7.62	—
XIII	C_2H_5	C_3H_7	65—67 (6)	1.4299	9	7.56	7.45, 7.46	157—158°
XIV	C_2H_5	C_4H_9	64—65 (4)		5	7.03	6.81, 6.62	116—116.5
XV	C_2H_5	Iso-C_5H_{11}	95—96 (4)	1.4322	10	6.57	6.44, 6.62	111.5—112

The picrate melted at 76° (twice recrystallized from methanol).

In a similar way we prepared methyl β-diethylaminoisobutyrate with b. p. 85-85.5° (25 mm), n_D^{20} 1.4281 (yield 85%) and methyl β-piperidinoisobutyrate with b. p. 89-90° (3 mm), n_D^{25} 1.4512 (yield 95%).

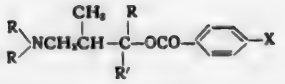
Aliphatic tertiary amino alcohols (I–X). The amino alcohols (I–X) were prepared by a general method. The preparation of 4-dimethylamino-2,3-dimethylbutanol-2 (I) is given as an example.

36.2 g of methyl β-dimethylaminoisobutyrate (b. p. 70-71° at 24 mm, n_D^{20} 1.4201) in 70 ml of absolute ether was added dropwise with vigorous stirring to methylmagnesium iodide, prepared from 14 g of magnesium and 71 g of methyl iodide in 380 ml of absolute ether cooled in ice and salt. The rate of addition of the amino ester was regulated so that the temperature of the reaction mixture did not rise above -5°. After the addition of all the amino ester, stirring was continued for 1 hour at room temperature and for two hours on a water bath at the boiling point of the ether. Then the reaction mixture was hydrolyzed with a saturated soda solution (50 ml) and extracted three times with ether. The ether extracts were dried with sodium sulfate, and after evaporation of the solvent, the residue was vacuum distilled. We obtained 26.5 g of 4-dimethylamino-2,3-dimethylbutanol-2 (I) with b. p. 59-60° (10 mm). The constants and yields of all the amino alcohols prepared are given in Table 1. In the preparation of the amino alcohols (IV, V, VIII, IX and X) by the method described, together with the amino alcohols we also isolated the amino ketones (XI–XV), whose constants and yields are given in Table 2.

3-Dialkylamino-2-methyl-1,1-diphenylpropanols (XVI, XVII and XVIII). The amino alcohols (XVI, XVII and XVIII) were prepared by the same method. As an example, the preparation of 3-dimethylamino-2-methyl-1,1-diphenylpropanol-1 (XVI) is described. 3 g of methyl β-dimethylaminoisobutyrate in 50 ml of of absolute ether was slowly added with vigorous stirring and cooling to the phenylmagnesium bromide prepared from 14 g of magnesium and 80 g of freshly distilled bromobenzene in 300 ml of ether. During the reaction, the temperature was kept below -5°. The mixture was kept overnight at room temperature, then the ether was distilled off, 250 ml of benzene added to the residue and the product hydrolyzed with 50 ml of concentrated soda solution. The benzene layer was separated, the residue washed twice with small portions of benzene (50 ml each) and the benzene extracts dried with sodium sulfate. After evaporation of the solvent, the residual thick oil was dissolved in 200 ml of 10% hydrochloric acid and the acid solution extracted with ether, filtered and made alkaline with soda. The precipitated crystals were filtered off and recrystallized from ethyl alcohol. We obtained 55 g (83%) of 3-dimethylamino-2-methyl-1,1-diphenylpropanol-1 (XVI) with m. p. 94-95°.

Found %: N 5.22, 5.34. $C_{18}H_{23}ON$. Calculated %: N 5.20.

TABLE 3

Esters 

No. of sample	R	R′	X	Boiling point of the base at given pressure (mm)	Melting point		Yield (in %)	Nitrogen yield (in %)	
					hydrochloride	oxalate		calc.	found
XXI	CH_3	CH_3	H	—	163—164°	—	57	4.94	5.27. 5.29
XXII	CH_3	C_2H_5	H	—	162—162.5	—	65	4.46	4.58. 4.64
XXIII	CH_3	C_3H_7	H	—	172—172.5	—	65	4.10	4.10. 4.17
XXIV	CH_3	C_4H_9	H	—	—	140—145°	76	3.31	3.52. 3.21
XXV	CH_3	Iso-C_5H_{11}	H	—	—	144—145	75	3.45	3.44. 3.57
XXVI	CH_3	CH_3	NO_2	—	214—214.5	—	79.5	8.47	8.57. 8.58
XXVII	CH_3	C_2H_5	NO_2	—	184.5—185	—	85	7.81	7.90. 8.09
XXVIII	CH_3	C_3H_7	NO_2	—	174—174.5	—	57	7.22	7.25. 7.39
XXIX	CH_3	C_4H_9	NO_2	—	142—143	—	89	6.75	6.54. 6.75
XXX	CH_3	Iso-C_5H_{11}	NO_2	—	Oil	—	80		
XXXI	CH_3	CH_3	NH_2	M.p. 123—123.5°	Dihydrochloride 169.5—170.5	—	73.5	10.60	10.50. 10.93
XXXII	CH_3	C_3H_7	NH_2	—	—	159.5—160	93	6.82	6.86. 6.70
XXXIII	CH_3	Iso-C_5H_{11}	NH_2	—	—	118—119	50	6.00	5.98. 5.80
XXXIV	C_2H_5	CH_3	H	—	—	125.5—127	49	3.82	4.10. 3.96
XXXV	C_2H_5	C_2H_5	H	103—107 (2.5)	—	—	25	4.59	4.58. 4.65
XXXVI	C_2H_5	C_3H_7	H	95—98 (1.5)	—	—	18	4.20	4.34. 4.35
XXXVII	C_2H_5	C_4H_9	H	85—87 (1)	—	—	25	3.87	4.10. 3.96
XXXVIII	C_2H_5	Iso-C_5H_{11}	H	91—93 (1)	—	—	23	3.59	3.32. 3.29
XXXIX	C_2H_5	CH_3	NO_2	—	170—170.5	—	75.5	7.81	7.48. 7.65
XL	C_2H_5	CH_3	NH_2	—	175—176	153.5—154	62.5	7.33	7.08. 7.28

The hydrochloride melted at 238-239° and the picrate at 82-83°.

Treatment of methyl β-diethylaminoisobutyrate with phenylmagnesium bromide by the method described gave a 78% yield of 3-diethylamino-2-methyl-1,1-diphenylpropanol-1 (XVII) with m. p. 79-79.5° (from ethanol).

Found %: N 4.80, 5.08. $C_{20}H_{27}ON$. Calculated %: N 4.71.

The hydrochloride of this amino alcohol melted at 141-142° (from ethanol).

Treatment of methyl β-N-piperidinoisobutyrate with phenylmagnesium bromide gave an 85% yield of 3-N-piperidino-2-methyl-1,1-diphenylpropanol-1 (XVIII) with m. p. 122-122.5° (from ethanol).

Found %: N 4.73, 4.75. $C_{21}H_{27}ON$. Calculated %: N 4.53.

3-Dimethylamino-2-methyl-1,1-diphenylpropene-1 (XIX). A mixture of 20 g of 3-dimethylamino-2-methyl-1,1-diphenylpropanol-1 (XVI), 40 ml of concentrated hydrochloric acid and 133 ml of glacial acetic acid was heated on a boiling water bath for 30 minutes and then left overnight. After removal of the water and acetic acid in vacuum, the residue was neutralized with alkali and the liberated oil extracted with ether and dried with sodium sulfate. After distilling off the ether and recrystallizing the residue from alcohol, we obtained 12 g of 3-dimethylamino-2-methyl-1,1-diphenylpropene-1 (XIX) with m. p. 56-56.5°.

Found %: N 5.66, 5.65. $C_{18}H_{21}N$. Calculated %: N 5.58.

The hydrochloride had m. p. 191-191.5°. The picrate had m. p. 172.5-173°.

3-Dimethylamino-2-methyl-1,1-diphenylpropane (XX). 3.2 g of 3-dimethylamino-2-methyl-1,1-diphenylpropene-1 (XIX), dissolved in 30 ml of ethyl alcohol, was hydrogenated at room temperature in the presence of skeletal nickel catalyst. 340 ml of hydrogen (instead of 305 ml, required theoretically) was absorbed. The catalyst was filtered off and after removal of the alcohol, the residue was vacuum distilled. We obtained 3 g of 3-dimethylamino-2-methyl-1,1-diphenylpropane (XX).

B. p. 142-142.5° (3 mm), n_D^{20} 1.5543, d_4^{20} 0.9865, MR 82.11; calc. 82.07.

Found %: N 5.50, 5.80. $C_{18}H_{23}N$. Calculated %: N 5.53.

The hydrochloride had m. p. 185.5-186°.

Esters of tertiary aliphatic amino alcohols (XXI–XL). The esters of the given amino alcohols were prepared in the form of the hydrochlorides, oxalates (if the hydrochloride could not be prepared) and free bases (if crystalline salts could not be prepared). As examples we describe the preparation of the amino ester hydrochloride (XXI), the amino ester oxalate (XXV) and the free base of the amino ester (XXXV).

The benzoate of 4-dimethylamino-2,3-dimethylbutanol-2 (XXI). 15.2 g of benzoyl chloride was gradually added to 10 g of 4-dimethylamino-2,3-dimethylbutanol-2 and 0.56 g of magnesium in 50 ml of anhydrous benzene. Heat was evolved during the reaction and after some time, a crystalline precipitate formed. The mixture was heated on a water bath at 85-90° for 30-50 minutes. After removal of the benzene in vacuum, an aqueous soda solution was added to the residue and the liberated oil was extracted several times with ether. The ether extract was dried with sodium sulfate and saturated with hydrogen chloride. We obtained 11 g (56.5%) of the benzoate of 4-dimethylamino-2,3-dimethylbutanol-2 (XXI) hydrochloride with m. p. 163-164° (from ethyl alcohol).

Found %: N 5.27, 5.29. $C_{15}H_{23}O_2N \cdot HCl$. Calculated %: N 4.91.

The benzoate of 1-dimethylamino-2,3,6-trimethylheptanol-3 (XXV). A mixture of 8 g of 1-dimethylamino-2,3,6-trimethylheptanol-3 (V), 0.4 g of magnesium, 50 ml of anhydrous benzene and 9.7 g of benzoyl chloride was heated for 50 minutes on a water bath at 85-90°. After removal of the benzene in vacuum, the residue was treated with an aqueous soda solution and the liberated oil extracted with ether (40 ml). The ether

extract was dried with sodium sulfate and to it was added an ether solution of oxalic acid. The precipitate was filtered off and recrystallized from ethyl alcohol. We obtained 10.5 g (75%) of the benzoate of 1-dimethylamino-2,3,6-trimethylheptanol-3 (XXV) oxalate with m. p. 144-145°.

Found %: N 3.45, 3.57. $C_{21}H_{33}O_6N$. Calculated %: N 3.45.

The benzoate of 1-diethylamino-2-methyl-3-ethylpentanol-3 (XXXV). A mixture of 8 g of 1-diethylamino-2-methyl-3-ethylpentanol-3 (VII), 0.5 g of magnesium, 50 ml of anhydrous benzene and 8.5 g of benzoyl chloride was heated for 40 minutes at 85-90°. After removal of the benzene in vacuum, the residue was treated with soda solution. The liberated oil was extracted with ether and dried with sodium sulfate. Saturating the ether solution with dry hydrogen chloride precipitated an oil, which could not be crystallized. The hydrochloride of the benzoate was reconverted into the free base by treatment with soda solution, extracted with ether, dried with sodium sulfate and vacuum distilled. We obtained 3 g of the benzoate of 1-diethylamino-2-methyl-3-ethylpentanol-3 (XXXV) with b. p. 103-107° (2 mm).

Found %: N 4.58, 4.65. $C_{19}H_{31}O_2N$. Calculated %: N 4.59.

We were also unable to prepare other crystalline salts of this ester (oxalate and tartrate). The constants of the other benzoates and p-nitrobenzoates and their derivatives, which were prepared in a similar way, are given in Table 3.

The p-aminobenzoate of 1-dimethylamino-2,3-dimethylhexanol-3 (XXXII). 5 g of the p-nitrobenzoate of 1-dimethylamino-2,3-dimethylhexanol-3 (XXVIII) hydrochloride in 50 ml of methyl alcohol was hydrogenated in an autoclave at 70-80° and a pressure of 20 atm. of hydrogen in the presence of a skeletal nickel catalyst. Three liters of hydrogen (2.9 liters was required according to calculation) was absorbed. The catalyst was filtered off, the solution evaporated down in vacuum, an aqueous solution of soda added to the residue and the liberated oil extracted with ether and dried with sodium sulfate. An ether solution of oxalic acid was added to the ether extract. We obtained 4.95 g of the p-aminobenzoate of 1-dimethylamino-2,3-dimethylhexanol-3 (XXXII) oxalate as an oil, which crystallized after many reprecipitations from alcohol with ether; the m. p. was 159.5-160°.

Found %: N 6.86, 6.70. $C_{19}H_{30}O_6N_2$. Calculated %: N 7.33.

The p-aminobenzoates (XXXI, XXXIII and LX) were prepared similarly and their constants and yields are given in Table 3.

SUMMARY

Starting with methyl methacrylate, we prepared a series of aliphatic and aliphatic-aromatic tertiary amino alcohols and their esters (benzoates, p-nitrobenzoates and p-aminobenzoates), which were tested pharmacologically. Some of the esters obtained possessed considerable anesthetic activity. p-Aminobenzoates in this series of compounds had a weaker anesthetic activity then the corresponding benzoates.

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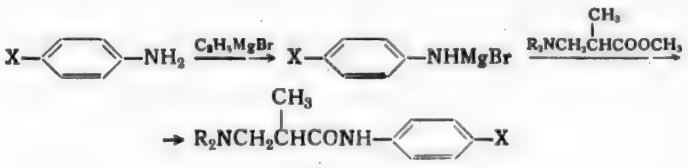
SYNTHETIC ANESTHETICS

XVIII. ANILIDES AND SUBSTITUTED AMIDES OF β-DIALKYLAMINOISOBUTYRIC AND SOME AROMATIC ACIDS

I. N. Nazarov* and L. Z. Kazaryan

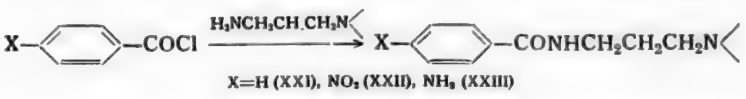
By treating esters of β-dialkylaminoisobutyric acids with a Grignard reagent we previously prepared a series of tertiary amino alcohols, which were then converted into aromatic esters, possessing noticeable anesthetic activity [1]. Lately it has been reported that, in certain cases, amides are more effective anesthetics than the corresponding esters [2]. We therefore synthesized a series of amides of β-dialkylaminoisobutyric acids in order to test them pharmacologically and compare their properties with those of the esters of amino alcohols we described previously. We prepared amides of the following three types: anilides of β-dialkylaminoisobutyric acids, substituted amides of β-dialkylaminoisobutyric acids and substituted amides of aromatic acids.

The anilides of β-dialkylaminoisobutyric acids (I–XV), given in Table 1, were synthesized by the following scheme



The substituted amides of β-dialkylaminoisobutyric acids (XVI–XX), given in Table 2, were synthesized by reacting methyl esters of β-dialkylaminoisobutyric acids with aminemagnesium bromides, prepared by treating piperidine and γ-diethylaminopropylamine with ethylmagnesium bromide.

Substituted amides of aromatic acids (XXI–XXII) were prepared by reacting γ-diethylaminopropylamine with benzoyl and p-nitrobenzoyl chlorides. The p-nitrobenzamide (XXII) was then reduced to the p-aminobenzamide (XXIII).



X=H (XXI), NO_2 (XXII), NH_2 (XXIII)

*Deceased.

The γ-diethylaminopropylamine required for the synthesis was prepared by adding diethylamine to acrylonitrile followed by hydrogenation of the β-diethylaminopropionitrile in an ammonia-saturated methanol medium, which made it possible to increase the diamine yield to 73% instead of the 38-63% given in the literature [3].

$$CH_2{=}CHCN \xrightarrow{(C_2H_5)_2NH} (C_2H_5)_2NCH_2CH_2CN \xrightarrow[(NH_3)]{H_2,\ Ni} (C_2H_5)_2NCH_2CH_2CH_2NH_2$$

Physiological tests* of the preparations (I, II, III, V, XI, XII, XIII and XV) showed that only the anilide (XI) had a noticeable anesthetic activity equal to that of novocaine. All the other preparations investigated had no anesthetic activity, but did have a certain spasmolytic activity.

EXPERIMENTAL

The methyl esters of β-dimethylamino-, β-diethylamino- and β-piperidino- isobutyric acids were prepared as we described previously [1].

p-Butoxyacetanilide. 37.8 g of p-acetaminophenol was added to a solution of sodium methoxide, prepared from 8 g of sodium and 150 ml of anhydrous methanol. To the solution obtained was added 41 g of butyl bromide and the mixture was then heated on a water bath for 6 hours. The precipitated sodium bromide was filtered off, the bulk of the methanol distilled off and the residue diluted with water (200 ml). We obtained 42 g (81%) of p-butoxyacetanilide with m. p. 112°.

p-Butoxyaniline. A mixture of 40 g of p-butoxyacetanilide and 300 ml of 25% sulfuric acid was boiled and stirred vigorously for 1 hour, until the residue completely dissolved. The crystalline sulfate, which formed when the acid solution was cooled, was filtered off, mixed with 300 ml of water and treated with 100 ml of 15% sodium hydroxide, while stirred and heated (50-60°). The liberated oil was extracted with ether, dried with potash and vacuum distilled after removal of the ether. We obtained 23 g (85%) of p-butoxyaniline with b. p. 127-128° (8 mm), n_D^{20} 1.5335.

Anilides of β-dialkylaminoisobutyric acids. 9.5 g of freshly distilled aniline was added with cooling and stirring over a period of half an hour to the ethylmagnesium bromide prepared from 3 g of magnesium and 11 g of ethyl bromide in 250 ml of absolute ether. After 30-40 minutes, 14.5 g of methyl β-dimethylaminoisobutyrate (b. p. 70-71° at 24 mm) in 50 ml of absolute ether was added dropwise with stirring and cooling in ice to the solution of anilinemagnesium bromide formed. The mixture was kept at room temperature for 2 hours, then hydrolyzed with 50 ml of water and extracted with ether. The ether extracts were dried with sodium sulfate and the residue from evaporation of the ether distilled in vacuum. We obtained 18.2 g (88.3%) of the anilide of β-dimethylaminoisobutyric acid (I) as a thick, light yellow liquid with b. p. 145-146° (4 mm).

Found %: N 13.43, 13.31. $C_{12}H_{18}ON_2$. Calculated %: N 13.59.

The hydrochloride had m. p. 137-138°

In a similar way we prepared the anilides (II–XV), whose constants and yields are given in Table 1. For the anilides (VI–X), which contained the diethylamino group, we were unable to prepare crystalline hydrochlorides.

β-Diethylaminopropionitrile. With stirring and cooling, 100 g of acrylonitrile was added over a period of 40 minutes to 146 g of diethylamine. The reaction mixture was heated to 70° and left overnight. Vacuum distillation yielded 240 g (95.2%) of β-diethylaminopropionitrile with b. p. 93-93.5° (21 mm).

γ-Diethylaminopropylamine. 240 g of β-diethylaminopropionitrile in 500 ml of 12% ammonia in methanol was hydrogenated for 2 hours in an autoclave at 115° with an initial hydrogen pressure of 100 atm. using a skeletal nickel catalyst. 84.9 liters of hydrogen was absorbed (85.29 liters calculated). The catalyst was filtered off and the methanol solution distilled to give 182 g (73.5%) of γ-diethylaminopropylamine with b. p. 168-168.5°, n_D^{20} 1.4356.

* The physiological tests were carried out in the pharmacological laboratories of the S. Ordzhonikidze All-Soviet Sci. Res. Inst. of Chem. and Pharm., under the direction of M. D. Mashkovsky.

TABLE 1

Anilides $R_2NCH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCONH-C_6H_4-X$

Substance No.	R_2N	X	Boiling point at the given pressure (mm)	Yield (in %)	Melting point of hydrochloride	Nitrogen content (in %)	
						calc.	found
(I)	$(CH_3)_2N$	H	145—146° (4)	88.3	137—138°	13.59	13.43. 13.31
(II)		CH_3	158—159 (2)	69.5	171—171.5	12.72	12.60. 12.75
(III)		OCH_3	172—174 (1)	60.5	179—179.2	11.86	11.99. 11.90
(IV)		OC_4H_9	195—196 (2)	69	153—153.2	10.09	9.90. 10.00
(V)		OC_5H_{11}-iso	205—206 (2)	65	139—140	9.59	9.43. 9.64
(VI)	$(C_2H_5)_2N$	H	167—168 (1.5)	66.2	—	11.96	11.73. 11.68
(VII)		CH_3	165—166 (1)	65.3	—	11.29	11.28. 11.10
(VIII)		OCH_3	175—176 (1)	60.9	—	10.60	10.48. 10.18
(IX)		OC_4H_9	207—208 (2)	75.1	—	9.15	9.00. 9.26
(X)		OC_5H_{11}-iso	210—212 (0.5	75.2	—	8.75	8.98. 9.00
(XI)	$C_5H_{10}N$	H	176—177 (1)	62.2	Sulfate 103—104	11.36	11.0. 11.34
(XII)		CH_3	205—207 (1)	63	181—181.5	10.77	10.78. 10.99
(XIII)		OCH_3	208—210 (1)	55.7	186—187	10.14	10.42. 10.48
(XIV)		OC_4H_9	231—233 (3)	65.5	156—156.5	8.80	8.37. 8.58
(XV)		OC_5H_{11}-iso	224—225 (1)	42.2	179—180	8.43	8.73. 8.45

TABLE 2

Substituted amides $R_2NCH_2CH(CH_3)CONHAm$

Substance No.	R_2N	Am	Boiling point at given pressure (mm)	Yield (in %)	Nitrogen content (in %)	
					calc.	found
(XVI)	$(CH_3)_2N$	$(C_2H_5)_2N(CH_2)_3NH$	138° (12)	53.9	16.91	17.10. 16.73
(XVII)	$(CH_3)_2N$	$C_5H_{10}N$	115—116 (3)	69.6	14.14	13.60. 13.56
(XVIII)	$(C_2H_5)_2N$	$C_5H_{10}N$	129—130 (3)	75.2	12.39	12.36. 12.51
(XIX)	$C_5H_{10}N$	$C_5H_{10}N$	153—154 (2)	77.2	11.76	11.96. 11.73
(XX)	$C_5H_{10}N$	$(C_2H_5)_2N(CH_2)_3NH$	173—174 (3)	61.8	14.84	14.72. 15.10

Footnote. The melting point of the hydrochloride of the substance (XIX) was 203°.

γ-Dimethylaminopropylamide of β-dimethylaminoisobutyric acid (XVI). 13 g of γ-diethylaminopropylamine in 50 ml of absolute ether was added dropwise with vigorous stirring and cooling to the ethylmagnesium bromide prepared from 3 g of magnesium and 11 g of ethyl bromide in 150 ml of absolute ether. After 30 minutes, 14.5 g of methyl β-dimethylaminoisobutyrate in 50 ml of ether was added dropwise with stirring and cooling to the γ-diethylaminopropylaminemagnesium bromide prepared. After standing for 3 hours at room temperature, the mixture was hydrolyzed with 50 ml of water and extracted with ether. The ether extracts were dried with sodium sulfate. Distillation gave 13.1 g (54%) of the γ-diethylaminopropylamide of β-dimethylaminoisobutyric acid (XVI) as a light yellow oil with b. p. 138° (12 mm).

Found %: N 17.1, 16.73. $C_{13}H_{29}ON_3$. Calculated %: N 16.91.

In a similar way we prepared the substituted amides of β-diethylamino- and β-piperidinoisobutyric acids (XVII—XX), given in Table 2.

γ-Diethylaminopropylamide of benzoic acid (XXI). 35 g of γ-diethylaminopropylamine was added to a solution of 29 g of benzoyl chloride in 50 ml of anhydrous benzene, which was cooled with water and stirred. The reaction mixture was heated on a water bath for 1 hour, then cooled and acidified with 10% hydrochloric acid (150 ml). The acid, aqueous solution was separated from the benzene layer and neutralized with soda (to litmus). The liberated oil was extracted with ether, dried with sodium sulfate and vacuum distilled, after evaporation of the ether. We obtained 39.7 g (94.4%) of the γ-diethylaminopropylamide of benzoic acid (XXI) as a thick colorless oil with b. p. 185° (3 mm), which became yellow on standing.

Found %: N 12.22, 12.17. $C_{14}H_{22}ON_2$. Calculated %: N 11.96.

γ-Diethylaminopropylamide of p-nitrobenzoic acid (XXII). 35 g of γ-diethylaminopropylamine was added to a solution of 46.3 g of p-nitrobenzoyl chloride in 50 ml of dry benzene, which was stirred and cooled with water. The reaction mixture was heated for 2 hours on a water bath and then cooled and acidified with 10% hydrochloric acid (300 ml). The acid, aqueous solution was separated from the benzene layer, neutralized with soda (to litmus) and the liberated oil extracted with ether. The ether extracts were dried with sodium sulfate. The residue after evaporation of the ether and unreacted γ-diethylaminopropylamine was a thick oil, which would not distil in vacuum. The oil obtained (71 g) was dissolved in 500 ml of 10% sulfuric acid at 60° and the solution saturated with sodium chloride, filtered and left overnight. The crystals formed were filtered off and dried in air. We obtained 65.6 g (80%) of the γ-diethylaminopropylamide of p-nitrobenzoic acid sulfate with m. p. 174°. The sulfate was dissolved in 400 ml of water, neutralized with 20% soda solution and the liberated oil extracted with ether. The ether extract was dried with sodium sulfate and saturated with dry hydrogen chloride. We obtained 60.4 g of γ-diethylaminopropylamide of p-nitrobenzoic acid hydrochloride, which was purified by reprecipitation from methanol with ether and melted at 180-181°.

Found %: N 11.64, 11.59. $C_{14}H_{21}O_3N_3$. Calculated %: N 11.25.

γ-Diethylaminopropylamide of p-aminobenzoic acid (XXIII). 26 g of the γ-diethylaminopropylamide of p-nitrobenzoic acid hydrochloride in 150 ml of methanol was hydrogenated for 3 hours in an autoclave at 70° with an initial hydrogen pressure of 92 atm in the presence of 5 g of skeletal nickel catalyst. 5.1 liters of hydrogen were absorbed (5.51 liters were required according to calculation). The catalyst was filtered off and the residue after evaporation of the methanol made slightly alkaline (to litmus) with soda solution. The liberated oil was extracted with ether and dried with sodium sulfate. After distilling off the ether and distilling the residue in vacuum, we obtained 18.2 g (87.5%) of the γ-diethylaminopropylamide of p-aminobenzoic acid as a thick oil with b. p. 252-253° (3 mm), which crystallized on adding several drops of absolute ether and melted at 125°

Found %: N 16.95, 17.06. $C_{14}H_{23}ON_3$. Calculated %: N 16.87.

SUMMARY

A series of anilides and substituted amides of β-dialkylaminoisobutyric and benzoic acids were synthesized in order to test them pharmacologically. Of the compounds obtained, only the anilide of β-N-piperidinoisobutyric acid had a noticeable anesthetic activity (equal to that of novocaine).

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ELECTROREDUCTION AS A METHOD FOR INVESTIGATING PROTEIN

I. STUDY OF SUBSTANCES FORMED BY THE ELECTROREDUCTION OF CERTAIN DIKETOPIPERAZINES

T. I. Orlova and N. I. Gavrilov

One of the methods for studying the structures of proteins is based on the electroreduction of diketopiperazines to piperazines at a mercury cathode [1]. Piperazine is also formed from diketopiperazines by electroreduction at a lead cathode [2], by reduction with metallic sodium in alcohols [3], and with lithium aluminum hydride [4]. Heimrod observed the formation of aminoaldehydes in the electroreduction of diketopiperazines at a mercury cathode [5]. Apparently, the diketopiperazine ring was thus broken. However, in this case the conditions of reduction were different from those in the method proposed by N. I. Gavrilov and A. V. Koperina [1], in that Heimrod used a high concentration of diketopiperazine and carried out the reduction at a very low cathode temperature.

We continued our investigations on the electroreduction of diketopiperazines at a mercury cathode, studied the substances formed more thoroughly using paper chromatography, and also isolated the piperazines and proved their structures.

The composition of the cathode liquid during diketopiperazine electoreduction was investigated using the reduction of glycine anhydride and glycylphenylalanine anhydride. Samples of the cathode liquid taken 3 and 6 hours after the reduction started were chromatographed on "Leningrad" chromatography paper in a solvent system of butanol – 25% acetic acid in a 1:1 ratio.

The chromatogram of the electroreduction of glycine anhydride shows (Fig. 1) that the cathode solution contained very little glycylglycine, glycine anhydride and possibly glycine, after 3 and 6 hours of piperazine reduction. The presence of glycylglycine may be explained by the quite high hydrolizability of glycine anhydride in an acid medium during the reduction.

It was also shown chromatographically that the hydrolyzates of the cathode solutions, after diketopiperazine reduction, contained the corresponding amino acids and piperazines but did not contain any other products: alanine and 2,5-dimethylpiperazine in alanine anhydride reduction; glycine, alanine and 2-methylpiperazine in glycylalanine anhydride reduction; glycine, phenylalanine and 2-benzylpiperazine in the reduction of glycylphenylalanine anhydride (Figs. 2, 3, 4).

The formation of piperazines during reduction was proved not only chromatographically, but also by the isolation of piperazine picrates and dinitrophenyl derivatives of piperazines, which were then compared with the derivatives of authentic piperazines.

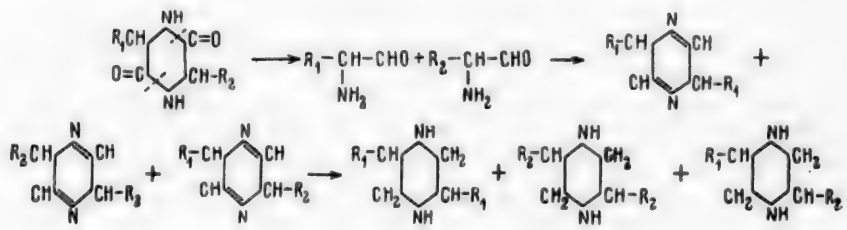
The dinitrophenyl derivatives of piperazines, which may be used for characterizing piperazines, are of particular interest. We first prepared them by treating piperazines with 1-fluoro-2,4-dinitrobenzene. The literature describes only 1,4-di-(2',4'-dinitro)-piperazine, prepared by treating piperazine with 1-chloro-2,4-dinitrobenzene [6].

1-Fluoro-2,4-dinitrobenzene reacted with piperazine at room temperature and with piperazine homologs at 40-50°, in the presence of sodium bicarbonate.

The dinitrophenyl derivatives of piperazine differ radically from the dinitrophenyl derivatives of amino acids, amino alcohols and primary and secondary amines. They are completely insoluble in water, alcohol, ether and other organic solvents, are noticeably soluble only in pyridine, dimethylformamide and concentrated sulfuric acid and during electrophoresis on paper are not displaced from the point of application either in an acid or alkaline buffer.

We isolated similar compounds by treating cathode solutions, after diketopiperazine electroreduction, with 1-fluoro-2,4-dinitrobenzene.

It is interesting to examine the electroreduction of diketopiperazines consisting of two different amino acids in more detail. If the electroreduction of such diketopiperazines to piperazines, under the conditions described by N. I. Gavrilov and A. V. Koperina, proceeded with cleavage of the diketopiperazine ring, as suggested by Heimrod, then a mixture of three piperazines instead of the one expected would be obtained during the formation of the piperazine ring.



We showed chromatographically that electroreduction of mixed diketopiperazines gave only the one piperazine expected. An ascending chromatogram (Fig. 5) using the system pyridine—acetic acid—water in a 50:35:15 ratio showed that the 2-methylpiperazine and 2-benzylpiperazine prepared by the electroreduction of glycylalanine anhydride and glycylphenylalanine anhydride, respectively, were individual substances and did not contain traces of other piperazines. This indicated that no cleavage of the diketopiperazine ring occurred in the electroreduction of diketopiperazines and that amino aldehydes could not be the precursors of piperazines.

As there is an extremely clear separation of piperazines on a paper chromatogram with the given system of solvents, this system is recommended for the chromatographic analysis of piperazines.

EXPERIMENTAL

1. Syntheses of diketopiperazines. In addition to the constants, we report the partition coefficients on descending paper chromatograms using the solvent system n-butanol — 25% acetic acid in a ratio of 1:1.

Glycine anhydride was prepared by Fischer's method [7] and had m. p. 310°; R_f = 0.41; according to data in [15]: m. p. 310-312°.

Alanine anhydride was prepared by Sannie's method [8],and had m. p. 277°; R_f = 0.72; according to [16]: m. p. 280°.

Glycylalanine anhydride. a) The ethyl ester of carbobenzoxyglycylalanine was synthesized by Boissonas's method [9] from 3.5 g of carbobenzoxyglycine and 2.7 g of the ethyl ester of alanine hydrochloride. The substance was isolated as an oil.

b) The ethyl ester of glycylalanine hydrobromide was prepared by treating the ethyl ester of carbobenzoxyglycylalanine at room temperature with 10 ml of glacial acetic acid, saturated with hydrogen bromide. When the evolution of carbon dioxide ceased, the solution was poured into 200 ml of water. The oil liberated (the hydrobromide of the dipeptide ester) was washed several times with ether. c) Glycylalanine anhydride: an alcohol solution of the dipeptide hydrobromide, saturated with ammonia at 0°, was left over night at room temperature, the alcohol evaporated off in vacuum and the residue washed on a filter with methyl alcohol to remove

NH_4Br and recrystallized from aqueous alcohol. The weight was 1.5 g. The substance did not give a ninhydrin reaction, did not contain halogen and was chromatographically pure.

M. p. 241°; R_f = 0.58; according to data in [10]; m. p. 240-244°.

Found %: N 21.85, 21.82. $C_8H_8O_2N_2$. Calculated %: N 21.87.

Glycylphenylalanine anhydride. a) The ethyl ester of carbobenzoxyglycylphenylalanine was prepared by Boissonas's method from 1.9 g of carbobenzoxyglycine and 2.5 g of the ethyl ester of phenylalanine hydrochloride. The substance was isolated as an oil. b) The ethyl ester of glycylphenylalanine was prepared by hydrogenation over a Pd catalyst for 4 hours in 20 ml of methyl alcohol, 1.5 ml of acetic acid and 1 ml of water. The solution was filtered free from catalyst and evaporated down to a sirup in vacuum. c) A solution of the dipeptide ester in 15 ml of ethyl alcohol was heated for 3 hours on a water bath and cooled. The white material which precipitated was filtered off and washed with water, alcohol and ether. We obtained 0.8 g of glycylphenylalanine anhydride. The substance did not give a ninhydrin reaction.

M. p. 279-280°; R_f = 0.90; according to data in [11]; m. p. 280-281°.

Found %: N 13.82, 13.71. $C_{11}H_{12}O_2N_4$. Calculated %: N 13.72.

2. Synthesis of piperazines. 2,5-Dimethylpiperazine [12] was prepared by hydrogenating 5 g of isonitrosoacetone in 20 ml of glacial acetic acid over a Pt catalyst for 15 hours. The catalyst was separated off by centrifuging and the acetic acid evaporated in vacuum. The residual oil was treated with dry acetone. The precipitate was recrystallized from aqueous acetone. The weight of the 2,5-dimethylpiperazine diacetate was 2 g. The m. p. was 183-185°, R_f = 0.70 (pyridine : acetic acid : water).

Found %: N 12.07, 12.18. $C_{10}H_{22}O_4N_2$. Calculated %: N 11.96.

The picrate had m. p. 300° (decomp.).

Found %: N 19.50, 19.45. $C_{18}H_{20}O_{14}N_8$. Calculated %: N 19.50.

2-Methylpiperazine was synthesized by Abdergalden's method [3] with slight changes. 1.5 g of finely divided metallic sodium was added quickly to a solution of 600 ml* of alanylglycine anhydride in 50 ml of alcohol. The cooled solution was diluted with 50 ml of water, the alcohol distilled off in vacuum and the aqueous solution extracted with chloroform (200 ml). The chloroform solution was extracted with 250 ml of 5% HCl in 5 portions. The hydrochloric acid was distilled off in vacuum, the residue dissolved in 5 ml of water and the picrate of 2-methylpiperazine precipitated by adding 10 ml of a saturated aqueous solution of picric acid.

The weight of the picrate was 25 mg. The m. p. was 275°. According to data in [13]: m. p. 276-278°. The substance was chromatographically pure and had R_f = 0.57 in the solvent system pyridine – acetic acid – water in the ratio 50:35:15.

3. Synthesis of dinitrophenyl derivatives of piperazines. 1,4-Di-(2',4'-dinitrophenyl)-piperazine. We anhydrous, commercial piperazine, which was recrystallized from alcohol and had m. p. 103°. 0.2 g of piperazine, 0.9 g of $NaHCO_3$, 0.9 g of 1-fluoro-2,4-dinitrobenzene in 10 ml of water and 5 ml of alcohol were shaken on a rocker for 3 hours. The yellow precipitate was filtered off and washed with hot water, alcohol and ether until the filtrate became colorless. The weight was 0.95 g (98%).

Electrophoresis was carried out on paper in 30% acetic acid and in 25% pyridine; in both cases the yellow spot did not move from the point of application (it did not contain acid or basic groups). The m. p. was 255-258° (decomp.). according to [6]: m. p. 240° (decomp.).

Found %: N 20.20, 19.65; C 45.93, 46.07; H 3.30, 3.39. $C_{18}H_{14}O_8N_6$. Calculated %: N 20.07; C 45.93; H 3.38.

1,4-Di-(2',4'-dinitrophenyl)-2,5-dimethylpiperazine. 50 mg of 2,5-dimethylpiperazine diacetate, 0.9 g

* As in original. 600 mg is more likely – Publisher's note.

of $NaHCO_3$ and 0.9 g of 1-fluoro-2,4-dinitrobenzene in 10 ml of water and 5 ml of alcohol was shaken for 3 hours at 40-50° and then for 3 hours at room temperature. The yellowish red precipitate was filtered off and washed with hot water, alcohol and ether until the filtrate became colorless. The weight was 81 mg (85%). The m. p. was 292-294° (decomp.).

Found %: N 18.67, 18.41; C 48.79, 48.84; H 4.15, 4.18. $C_{16}H_{12}O_8N_8$. Calculated %: N 18.83; C 48.43; H 4.07.

The dinitrophenyl derivatives of piperazine and dimethyl piperazine prepared were completely insoluble in water, alcohol, ether and other organic solvents. They were soluble in pyridine, dimethylformamide and concentrated sulfuric acid.

4. Electroreduction of diketopiperazines and chromatographic investigation of the reduction products. For electroreduction we used carefully purified, chromatographically pure diketopiperazines. The chromatographic analysis involved descending chromatography in the system butanol – 25% acetic acid in the ratio 1:1. The position of the spots on the chromatograms was determined using benzidine [14].

The electroreduction of glycine anhydride was carried out in the apparatus described in [1] using a mercury cathode 70.8 cm^2. A constant potential of 120 V and a current density of 50-55 $\mu A/cm^2$ were used. The mercury was redistilled in vacuum. 5% HCl (distilled) was used for the cathode and anode solutions. 100 mg of glycine anhydride was dissolved at room temperature in 50 ml of 5% HCl and reduced with the cathode liquid at 15-25° for 6-7 hours; after 3 and 6 hours reduction, samples of the cathode liquid were removed with a pipette and chromatographed (Fig. 1). The cathode solution was evaporated to dryness in vacuum and the residue dissolved in 10 ml of water. The solution obtained was divided into 2 parts.

Piperazine picrate. 10 ml of a saturated, aqueous solution of picric acid was added to 5 ml of the solution and the mixture boiled. The precipitate, which separated on cooling, was filtered off, washed with alcohol and ether and recrystallized from water. It decomposed at about 300° like the picrate of commercial piperazine and a mixture of the two preparations.

Found %: N 20.62, 20.40; C 35.60, 35.67; H 3.05, 3.04. $C_{16}H_{16}O_{14}N_8$. Calculated %: N 20.58; C 35.29; H 2.96.

Dinitrophenyl derivative of piperazine. 5 ml of the solution was neutralized with a small amount of solid $NaHCO_3$ and then a further 0.5 g of $NaHCO_3$ and 0.5 g of 1-fluoro-2,4-dinitrobenzene in 5 ml of alcohol were added and the mixture shaken for 3 hours on a rocker and the yellow precipitate filtered off, washed on the filter with hot water, alcohol and ether and recrystallized from aqueous pyridine. The m. p. was 255-260° (decomp.).

1,4-Di-(2',4'-dinitrophenyl)-piperazine, prepared from commercial piperazine, had m. p. 255-258° (decomp.). The melting point of a mixed sample was 254-258° (decomp.). According to solubility in organic solvents, it was also the same as the appropriate derivative of authentic piperazine.

Found %: N 19.85, 20.11. $C_{16}H_{14}O_8N_8$. Calculated %: N 20.07.

Electroreduction of alanine anhydride. 100 mg of alanine anhydride was dissolved in 50 ml of 5% HCl. The electroreduction was carried out as in the case of glycine anhydride. The cathode solution was diluted with 50 ml of conc. HCl and then boiled for 10 hours. The hydrolyzate was evaporated in vacuum and the residue dissolved in 10 ml of water (solution No. 1). A chromatogram of the hydrolyzate is shown in Fig. 2.

The picrate of 2,5-dimethylpiperazine was isolated from 5 ml of solution No. 1 by method described previously. The m. p. was 300° (decomp.). The picrate of 2,5-dimethylpiperazine, prepared by hydrogenating isonitrosoacetone, decomposed at 300°. The melting point of a mixed sample was not depressed.

Found %: N 19.53, 19.55; C 37.92, 37.93; H 3.65, 3.52. $C_{18}H_{20}O_{14}N_8$. Calculated %: N 19.56; C 37.76; H 3.52.

1,4-Di-(2',4'-dinitrophenyl)-2,5-dimethylpiperazine. To 5 ml of solution No. 1 was added 0.5 g of $NaHCO_3$ and 0.5 g of 1-fluoro-2,4-dinitrobenzene in 5 ml of alcohol. The mixture was heated on a water bath at 40-50° for 4 hours. The precipitate was filtered off and washed on the filter with hot water, alcohol and ether. The yellow-orange substance had m. p. 292-294° (with vigorous decomposition).

The dinitrophenyl derivative of authentic 2,5-dimethylpiperazine had m. p. 292-294° (with vigorous decomposition). The melting point of a mixed sample was 292° (with vigorous decomposition). According to solubility in organic solvents, the substance was also the same as the dinitrophenyl derivative of 2,5-dimethylpiperazine, prepared by hydrogenation of isonitrosoacetone.

Found %: N 18.86, 18.76. $C_{18}H_{18}O_8N_8$. Calculated %: N 18.83.

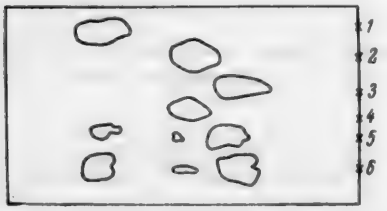


Fig. 1. 1) Glycine anhydride; 2) glycine; 3) piperazine; 4) glycylglycine; 5) cathode solution after 6 hours reduction; 6) cathode solution after 3 hours reduction.

Electroreduction of glycylalanine anhydride. 100 mg of the anhydride was reduced under the conditions described for the reduction of glycine anhydride. The cathode liquid was worked up in the same way as is the case of alanine anhydride. A chromatogram of the hydrolyzate is illustrated in Fig. 3.

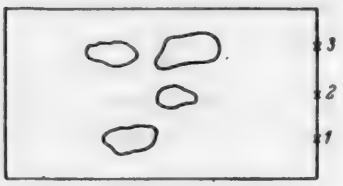


Fig. 2. 1) Alanine; 2) 2,5-dimethylpiperazine; 3) hydrolyzate of cathode liquid.

Picrate of 2-methylpiperazine. 5 ml of a saturated aqueous solution of picric acid was added to 5 ml of the solution after the hydrolysis to give the picrate of 2-methylpiperazine. The m. p. was 275-276°. The picrate of 2-methylpiperazine, prepared by Abdergalden's method, had m. p. 275°. The melting point of a mixed sample was 275-276°.

Found %: N 19.79, 19.70; C 36.67, 36.55; H 3.28, 3.34. $C_{17}H_{18}O_{14}N_8$. Calculated %: N 20.08; C 36.56; H 3.25.

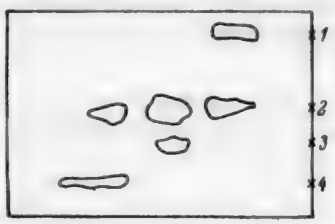


Fig. 3. 1) Glycine; 2) hydrolyzate of cathode solution; 3) 2-methylpiperazine; 4) alanine.

1,4-Di-(2',4'-dinitrophenyl)-2-methylpiperazine was obtained from 5 ml of the solution after the hydrolysis, 0.5 g of $NaHCO_3$ and 0.5 g of 1-fluoro-2,4-dinitrobenzene in 5 ml of alcohol by the method described for 2,5-dimethylpiperazine. The yellow-orange substance had m. p. 213° (vigorous decomposition). According to solubility in organic solvents, it was identical with dinitrophenyl derivatives of piperazines already described above.

Found %: N 19.37, 19.54. $C_{17}H_{16}O_8N_8$. Calculated %: N 19.44.

Electroreduction of glycylphenylalanine anhydride. 100 mg of the anhydride was reduced by the method described above.

Picrate of 2-benzylpiperazine. The cathode solution was evaporated to dryness in vacuum and the residue dissolved in 10 ml of water. The picrate was precipitated from 5 ml of the solution. The m. p. was 258-263°.

Found %: N 17.56, 17.52. $C_{23}H_{22}O_{14}N_8$. Calculated %: N 17.66.

1,4-Di-(2',4'-dinitrophenyl)-2-benzylpiperazine was prepared from 5 ml of the solution by the method described. The m. p. was 203-207°. According to solubility in organic solvents, it was identical with the dinitrophenyl derivatives of other piperazines.

Found %: N 16.70, 16.71. $C_{23}H_{20}O_8N_6$. Calculated %: N 16.72.

A chromatogram of the hydrolyzate of the cathode liquid is illustrated in Fig. 4.

5. Chromatography of piperazines. To separate the piperazines we used ascending chromatography on "Leningrad" chromatography paper. The mobile phase was the solvent system pyridine – acetic acid – water in the ratio 50:35:15. A horizontal pencil line (line of application) was drawn 3.5 cm from the lower edge of a sheet of chromatography paper 35 cm long and 10 cm wide. Solutions of the piperazine picrates in formic acid were put onto this line with a capillary at equal distances from each other and dried. The sheets were suspended in a hermetically sealed chromatography cylinder so that their lower edges were immersed in the solvent, 0.5 cm from the bottom of the cylinder. The solvent moved up a sheet to a height of 25-30 cm from the line of application in 15-17 hours. The picric acid moved with the solvent front. The chromatogram was dried in air until the smell of pyridine disappeared and developed with benzidine [14]. The substances appeared as blue spots on a white background. The piperazines had the following partition coefficients (R_f: 2,5-dimethylpiperazine 0.70, 2-methylpiperazine 0.57, piperazine 0.44, 2-benzylpiperazine 0.82) (Fig. 5).

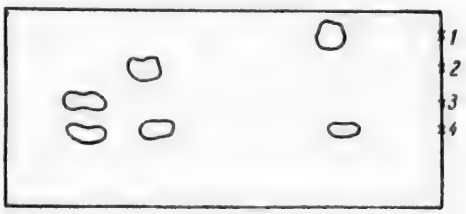


Fig. 4. 1) Glycine; 2) phenylalanine; 3) 2-benzylpiperazine; 4) hydrolyzate of cathode solution.

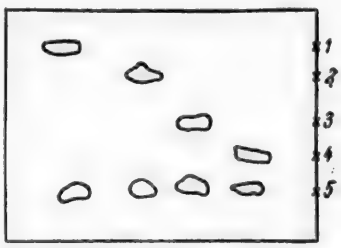


Fig. 5. 1) 2-benzylpiperazine; 2) 2,5-dimethylpiperazine; 3) 2-methylpiperazine; 4) piperazine; 5) mixture of piperazines.

SUMMARY

1. We investigated the electroreduction of the following diketopiperazines at a mercury cathode: glycine anhydride, alanine anhydride, glycylalanine anhydride and glycylphenylalanine anhydride.

2. It was shown that electroreduction of diketopiperazines gave piperazines. The piperazine structures were proved by preparing picrates and dinitrophenyl derivatives of piperazines and comparing their properties with those of the corresponding derivatives of authentic piperazines.

3. It was shown that piperazines cannot be formed through the stage of amino aldehyde formation.

4. A system of solvents is proposed for the chromatographic separation of piperazines.

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INVESTIGATION OF THE SYNTHESIS OF ORGANOSILICO COMPOUNDS

V. PREPARATION OF POLYSILOXANES WITH MIXED RADICALS

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In analogy with other compounds of high molecular weight, one can assume that the introduction of polar atoms, for example chlorine, into the methyl groups of the polysiloxane chain will affect the properties of the polysiloxanes obtained. In addition, chloroderivatives of this type could be used as starting materials for introducing other atoms and groups of atoms into the polysiloxane chain.

In order to determine the effect of polar substituents on the properties of polysiloxanes in this work, we prepared chloromethyl and dichloromethyl derivatives of methylsiloxanes by direct chlorination of appropriate methylchlorosilanes, using ultraviolet radiation followed by hydrolysis and polycondensation. An attempt was also made to prepare dimercaptanpolysiloxane, starting with the appropriate bis-chloromethylpolysiloxane.

1. Dimethyldichlorosilane was chlorinated according to literature data [1] by passing chlorine, dried with sulfuric acid, through a flask containing dimethyldichlorosilane, which was stirred and irradiated with ultraviolet light from a quartz lamp (PRK-4) placed inside the flask. The flask was cooled externally with ice water so that the temperature inside the flask was maintained within the range 10-20°. The hydrogen chloride evolved during the reaction was absorbed with water and the unreacted chlorine with 5% alkali. The amount of chlorine that reacted was determined by the increase in weight of the flask. The chlorination may be represented by the following equations:

$$(CH_3)_2SiCl_2 + Cl_2 \rightarrow CH_2Cl(CH_3)SiCl_2 + HCl, \quad (1)$$

$$CH_2Cl(CH_3)SiCl_2 + Cl_2 \rightarrow CHCl_2(CH_3)SiCl_2 + HCl, \quad (2)$$

$$CHCl_2(CH_3)SiCl_2 + Cl_2 \rightarrow CCl_3(CH_3)SiCl_2 + HCl. \quad (3)$$

The chlorination introduced 0.95 to 1.25 moles of chlorine per mole of dimethyldichlorosilane. The chlorination products were fractionally distilled twice using a fractionating column 45 cm high. The distillation gave two products whose properties were close to those of chloromethylmethyldichlorosilane and dichloromethylmethyldichlorosilane (see Table).

Properties of the Chloromethylderivatives Isolated

Hypothetical formula	Boiling point		Hydrolyzable chlorine content (in %)	
	according to literature data	found	calc.	found
$CH_2Cl(CH_3)SiCl_2$	122	121—125	43.4	43.0
$CHCl_2(CH_3)SiCl_2$	107 (225 mm)	142—151 (760 mm)	35.8	36.5

2. Preparation of polysiloxanes with mixed radicals and a study of their properties. Chloromethylmethyldichlorosilane was hydrolyzed with a water–alcohol mixture (1 : 1) in order to obtain cyclic polysiloxanes [2]. Washing with water resulted in a considerable loss of hydrolysis products due to their increased solubility, which apparently was connected with the increase in polarity of the polysiloxane molecules. In order to polycondense the chloro-containing hydrolysis products to the state of a highly viscous polymer, the products required heating for 12-15 hours at 150° with 4-5% concentrated sulfuric acid instead of the 4-6 hours with 2% conc. H_2SO_4 [2] at room temperature required by unsubstituted cyclic dimethylpolysiloxanes. Under these conditions the hydrolysis products darkened and carbonized. No polycondensation occurred with anhydrous ferric chloride [?] even on heating. There was no polycondensation either when the cyclic hydrolysis products were treated with dichloromethylmethyldichlorosilane.

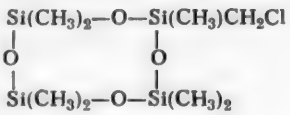
On hydrolyzing chloromethylmethyldichlorosilane with methyl alcohol [4] to obtain linear polysiloxanes, there was a decrease in hydrolysis product yield, also apparently due to the increase in solubility of the polar polysiloxanes in methanol. The linear hydrolysis products were more readily polycondensed than the cyclic ones; the former required heating with 3% conc. H_2SO_4 at a temperature of 80-85° for 4 hours.

The very high degree of stickiness of all the polycondensation products should be noted as this made the use of rollers for their treatment extremely difficult. The vulcanizates of the polycondensation products listed above were black, friable plates, occasionally perforated by pores. It was thus established that rubber-like products could not be obtained from pure chloroderivatives. In order to prepare the former, we synthesized polysiloxanes with mixed methyl and chloromethyl radicals in various proportions. In an attempted copolycondensation of the products of separate hydrolyses of dimethyldichlorosilane and chloromethylmethyldichlorosilane, they formed layers. The effect of the polarity of the chloromethyl radicals was also felt here; therefore the polysiloxanes of a mixed type were prepared by simultaneous methanol hydrolysis of mixtures of dimethyldichlorosilane and its chloroderivatives (up to 20%), taken in various proportions. In this case, also, there was a certain decrease in the yield of hydrolysis products due to their solubility in methyl alcohol, and the losses increased with an increase in the content of chlorinated products of the mixture [the yields of hydrolysis products were 73 to 86% instead of the 97-99% for pure $(CH_3)_2SiCl_2$].

There was a very slight retardation of the polycondensation of hydrolysis products with mixed radicals in the presence of conc. H_2SO_4 or anhydrous $FeCl_3$. The vulcanized products, prepared by the standard methods (with SiO_2 and TiO_2) had a somewhat lower tensile strength and smaller relative elongation. However, all chlorine-containing rubbers were found to have a higher coefficient of frost resistance: 0.96-1.07 at −55° and 100% elongation (instead of the 0.05-0.8 for pure dimethylpolysiloxane rubber) and a friability temperature below −100°. It is reported in the literature that the introduction of groups (chloromethyl, ethyl or phenyl) which destroy the regularity of the dimethylpolysiloxane chain causes an increase in the frost resistance of polysiloxane rubbers [5].

It was shown experimentally that during vulcanization there is a partial loss of chlorine or chloromethyl radicals apparently due to benzoyl peroxide. No losses of chlorine were observed under the same temperature conditions for the polycondensation products themselves (without benzoyl peroxide). An even greater decrease in the physico-mechanical characteristics of rubbers was noticed on using dichloromethyl radicals.

Octamethylcyclotetrasiloxane, isolated from the hydrolysis products of dimethyldichlorosilane, was also chlorinated. Chloromethylcyclotetrasiloxane was isolated from the chlorination products by distillation [6].



Rubber-like polysiloxanes were also obtained by simultaneous polycondensation with pure cyclotetrasiloxane.

3. Trimethylchlorosilane was chlorinated under the same conditions as dimethyldichlorosilane. 0.45 to

1.2 mole of chlorine were introduced per mole of trimethylchlorcsilane. The chlorination products were twice distilled on a fractionating column 50 cm high to give a product with b. p. 113-113.5° and containing 24.7% of hydrolyzable chlorine. According to literature data [1], chloromethyldimethylchlorosilane has b. p. 115° and contains a calculated 24.8% of hydrolyzable chlorine. The fraction with b. p. 147-150° from one distillation contained, apparently, $CHCl_2(CH_3)_2SiCl$ with b. p. 149.5° [1].

4. Chloromethyldimethylchlorosilane was hydrolyzed with distilled water. The reaction mixture had to be saturated with NaCl to isolate the hydrolysis products. The oil, dried with baked sodium sulfate, was distilled in vacuum (40 mm) and had b. p. 108°. The chlorine content, determined by sodium peroxide fusion in a bomb, was 30.5%, and that calculated for $CH_2Cl(CH_3)_2Si-O-Si(CH_3)_2CH_2Cl$, 30.75%.

Simultaneous polycondensation of the disiloxane prepared with octamethylcyclotetrasiloxane, taken in a 1:2 molar ratio, in the presence of 3% anhydrous ferric chloride and heating for 8 hours, gave a linear decasiloxane, blocked at the ends with chloromethyl groups: $CH_2Cl(CH_3)_2Si-[O-Si(CH_3)_2-]_8-O-Si(CH_3)_2CH_2Cl$. The chlorine content in such a siloxane was 8.6% calculated and 8.9% found.

Simultaneous methyl alcohol hydrolysis of a mixture of chloromethyldimethylchlorosilane and dimethyldichlorosilane, taken in a 1:2 molar ratio, gave a linear hexasiloxane, blocked at the ends with chloromethyl groups: $CH_2Cl(CH_3)_2Si-[-O-Si(CH_3)_2-]_4O-Si(CH_3)_2CH_2Cl$. The molecular weight of the product obtained, determined cryoscopically, was equal to 520, calculated 527.

An attempt was made to substitute the chlorine atoms in the terminal chloromethyl groups by SH groups. One of the experiments is given as a example: a solution of 40 g of bis-chloromethyltetramethyldisiloxane in 60 g of alcohol was added to a solution of 88 g of hyposulfite in 100 g of water. The mixture was heated at 140-150° for 14 hours and mixed until completely homogenized. 200 g of 50% H_2SO_4 was added and the heating continued for 4 more hours. The reaction mixture formed layers. On cooling, it was twice extracted with ether. The ether extract was washed with water, which was added to the lower layer. The amount of NaCl in the latter was determined. According to calculations 20.4 g of NaCl should form and 20.0 g (98%) was found. The ether was distilled off from the ether extract and the residue distilled in vacuum (37-38 mm). A considerable part of the product distilled in the range 120-126°. Analytical determination of dimercaptan in this fraction by argentometry with back titration of excess $AgNO_3$ with ammonium thiocyanate gave 90-100% dimercaptan. The mean molecular weight of this fraction, determined cryoscopically, was 239, whereas the theoretical molecular weight of the dimercaptan should be 226. It is possible that part of the SH group was oxidized and formed disulfide bonds.

SUMMARY

1. Direct chlorination of dimethyldichlorosilane and trimethylchlorosilane using ultraviolet light was carried out and individual chlorination products were isolated.

2. The chlorination products themselves and mixtures of them with dimethyldichlorosilane were hydrolyzed with methyl alcohol to give the corresponding linear polysiloxanes.

3. We established the high solubility of the hydrolysis products, containing chloromethyl radicals, in water and methanol. We also found that these products required more drastic conditions for polycondensation than pure dimethylsiloxanes.

4. It was found that the presence of chloromethyl groups in rubber-like polysiloxanes (up to 20 mole %) caused a certain deterioration in the physico-mechanical characteristics of the rubber, but considerably increased its frost resistance.

5. The possibility of substituting the chlorine atom in chloromethyl radicals by an SH group was demonstrated. Individual products were not isolated.

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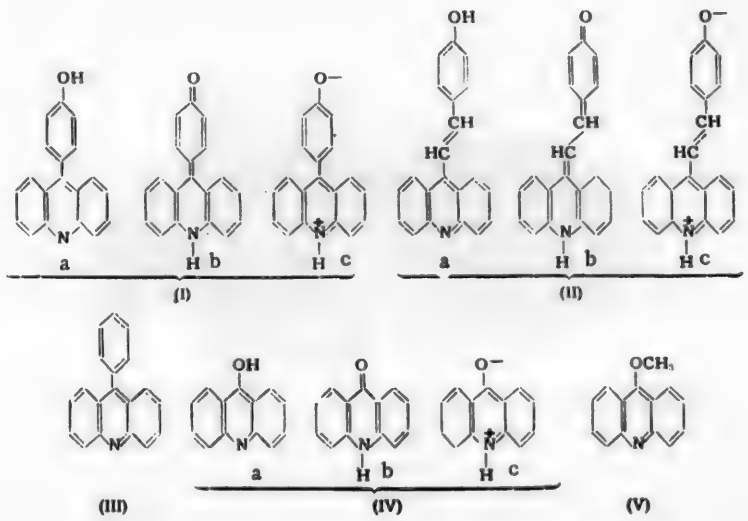
TAUTOMERISM OF ACRIDINE COMPOUNDS

STRUCTURE OF 9-(p-HYDROXYPHENYL)- AND 9-(p-HYDROXYSTYRYL)ACRIDINES

N. F. Kazarinova and I. Ya. Postovsky

In the present communication we discuss the investigation of the structure of 9-(p-hydroxyphenyl)acridine (I) [1] and 9-(p-hydroxystyryl)acridine (II). These compounds, despite the presence of phenolic radicals in them, are insoluble in dilute and concentrated alkalies. Both products are very difficultly soluble in concentrated hydrochloric acid and in organic solvents, and have a high melting point (>340°), in contrast to the compound without the hydroxyl group, namely 9-phenylacridine (III), which melts at 184° and is comparatively quite soluble in organic solvents and in concentrated hydrochloric acid.



In their properties compounds (I) and (II) resemble 9-hydroxyacridine (IVa), for which the tautomeric structure of the acridone (IVb) has been considered proved [2], although the structure of the betaine (IVc) is also probable [3].

On this basis it could be assumed that compounds (I) and (II) have the structure of the tautomeric oxo forms (Ib) and (IIb) corresponding to the acridone, or that they represent the betaines with structure (Ic) and (IIc).

A solution to the problem of the structure of compounds (I) and (II) is of interest for the theory of tautomeric transformations, since it permits ascertaining the influence exerted by the introduction of an additional conjugated system of phenyl and styryl bonds between the groups $>C=O$ and $>N-H$ or $-OH$ and $>N$ on the transfer of the mutual influence of these groups on the conjugation chain.

The properties of compounds (I) and (II) (insolubility in alkalies, etc.) speak in favor of the oxo structure. However, the following facts cannot be reconciled with the oxo structure. In the oxo forms (Ib) and (IIb) the phenyl radicals have a quinoid structure, and consequently it could be expected that these compounds, especially compound (IIb), will be deeply colored, similar to the recently described N-methyl derivative of quinone (IX), which represents dark purple needles [4]. In addition, a compound with the structure (Ib) should be unstable due to the steric hindrance offered to the arrangement of the quinone and acridan rings in one plane. Even in the case of the hydroxy structure (Ia) it is already impossible to have the phenyl and acridine rings in one plane, as can be seen from the space model of the compound, in that the spheres representing the hydrogen atoms are covered (Fig. 1). The presence of steric hindrance is even more probable in the case of the quinone (Ib), for the reason that a stable multiple bond between the quinone radical and the acridan nucleus can exist only with a planar arrangement of these rings, which is impossible when a double bond is present between them. The styryl compound (IIb) should differ from the phenyl compound (Ib) by a greater stability, since here the steric hindrance is smaller (Fig. 2). Actually, both products are equally quite stable compounds, and in addition to this, compound (I) is nearly colorless while compound (II) is colored yellow. Besides all of this, they give the methoxy derivatives with dimethyl sulfate in alkaline medium, and the acetoxy derivatives with acetic anhydride. On the basis of these data it is more probable for (I) and (II) to have either the hydroxy structure (a) or the inner ionic structure (c). However, this conclusion contradicts the insolubility of these compounds in alkalies and acids. To be sure, a detailed study revealed that compounds (I) and (II), suspended in either sodium hydroxide solution or in hydrochloric acid (1 : 1), go into solution even in the cold when a small amount of either dioxan or ethyl alcohol is added, imparting a bright orange color to the solution, whereas these same compounds are practically insoluble in either cold dioxan or alcohol, to the same extent that they are insoluble in either acid or alkali. *

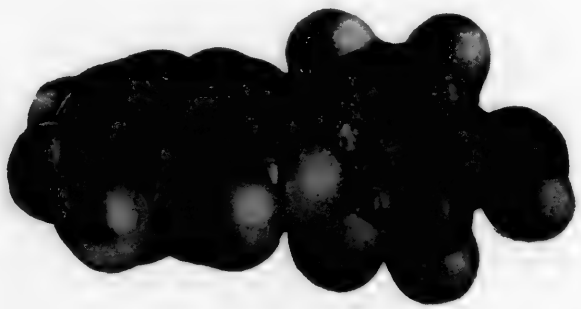
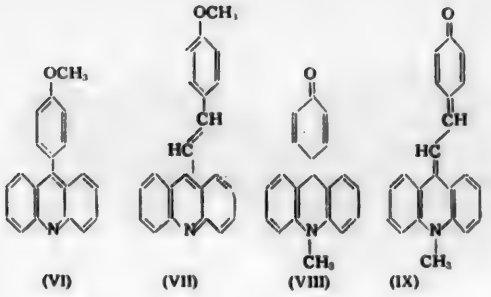


Fig. 1.

For these compounds to behave in such manner must indicate that stable intermolecular hydrogen bonds are present which mask the phenolic and basic properties of the compound. However, it is possible to assume stable intermolecular hydrogen bonds not only for the hydroxy form (a), but also for the oxo structure (b) and the inner structure (c). As a result, in order to solve the problem of the structure of (I) and (II) required further study. It seemed expedient to first compare compounds (I) and (II) with compounds having an authentic phenolic structure and an authentic quinoidal structure. For this purpose we synthesized 9-(p-methoxyphenyl)-acridine (VI) and 9-(p-methoxystyryl)acridine (VII), and also the quinones N-methyl-9-(p-benzoquino)acridan (VIII) and N-methyl-9-(p-benzoquinoethano)acridan (IX). Of these compounds 9-(p-methoxyphenyl)acridan (VI) and N-methyl-9-(p-benzoquinoethano)-acridan (IX) are described in the literature [4, 5].

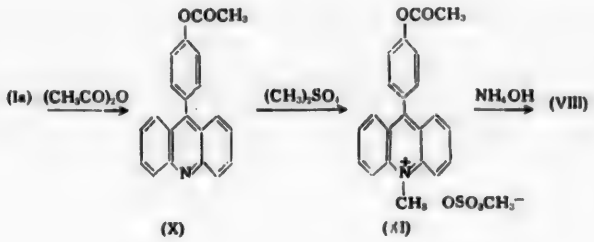
* This dissolving effect is especially noticeable if the compound if first suspended in dioxan, and then either caustic solution or acid is added.



(VI) (VII) (VIII) (IX)

In the present study compounds (I) and (VI) were synthesized by the condensation of diphenylamine with the corresponding p-hydroxy and p-methoxybenzoic acids by the Bernthsen method [6]. The 9-(p-methoxyphenyl)acridine (VI) obtained in this manner proved to be identical with the product obtained by the methylation of compound (I) with dimethyl sulfate. We obtained the styryl compounds (II) and (VII) by the method proposed by A. E. Porai-Koshits as early as 1907 for the synthesis of styryl derivatives of acridine [7], namely, by the condensation of 9-methylacridine with the proper aldehydes. The methoxy derivative obtained in this manner was identical with the product obtained by the methylation of compound (II).

Quinone (VIII) has not been described in the literature; we obtained it from the methosulfate (XI) of the acetyl derivative (X) by the following scheme



(X) (XI)

We will mention that in their properties the phenyl and styryl compounds (I, II and VI, VII) resemble each other very closely, from which it follows that in the styryl compounds (II) and (VII) there is good assurance of the transfer of mutual influence through the ethylenic group. In contrast to the starting compounds (I) and (II), the methoxy compounds (VI) and (VII) are quite readily soluble in organic solvents and in hydrochloric acid, and they also have comparatively lower melting points, namely 211-213° for (VI) and 191-193° for (VII).

Quinones (VIII) and (IX) also closely resemble each other in their properties, but both of them, as was to be expected, are entirely different from compounds (I) and (II). Both quinones are deeply colored (purple) compounds with well-defined solvation chromatic properties. The solution color of both of these quinones changes with increase in the polarity of the solvent from crimson to blue (positive solvation chromatism). When cooled in ice the color of the solutions deepens, and when heated—it becomes lighter.

The benzoquinoacridan (VIII) shows interesting properties. It is much more difficultly soluble in nonpolar solvents than quinone (IX). Its alcohol solutions rapidly decolorize on standing in the air. In the presence of alkali the decolorization takes place within a matter of several minutes, and it is easy to isolate N-methylacridone in 60% yield from the reaction medium. From this it follows that the spot most vulnerable to oxidation, where cleavage also occurs, is the double bond connecting the quinone and acridan rings. This is in full

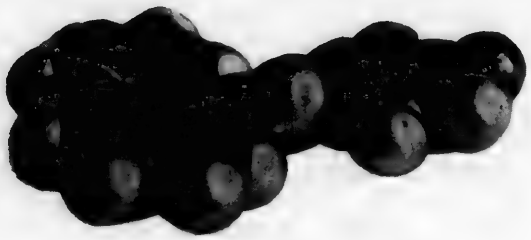


Fig. 2.

agreement with what has been said above regarding the difficulty of having the rings, connected by a double bond, in coplanar arrangement. In like manner the styryl quinone (IX), where the steric hindrance is smaller, remains unchanged under the conditions used to cleave the benzoquinoacridan (VIII).

A comparison of (I) and (II) with compounds having either an authentic phenolic structure or an authentic quinoidal structure permits rejecting the concept that the investigated compounds have an oxo structure, but at the same time it does not permit making a choice between the hydroxy structure (a) and the inner structure (c). We obtained additional data on the structure of compounds (I) and (II) by studying the polarograms of a number of acridine compounds. These data permitted making a more reliable choice between the two possible structures (a) and (b).

The reduction of acridine at a dropping mercury electrode at pH 8.4 gives two waves on the polarographic curve. Breyer and co-workers [8] attribute the first wave to the formation of the intermediate reduction product —the free radical (semiquinone), while the second wave corresponds to the final step of the reduction—the formation of dihydroacridine (acridan) compounds. Consequently, the potential of the first half-wave is especially characteristic for the compounds investigated by us. As can be seen from the data in the Table, acridine and 9-methoxyacridine resemble each other very closely in the character of their reduction. In turn, the half-wave potentials for acridone and N-methylacridone are also very close to each other; they give under the reduction conditions only one wave and differ from the first two compounds (1 and 2) in the character of their reduction. This difference is not observed for the phenyl compounds (5—7); they all show an $E_{1/2}$ close to the $E_{1/2}$ for 9-phenylacridine. In exactly the same manner the $E_{1/2}$ values for the styryl compounds (9—11) are also close to each other. The styryl derivatives are reduced more easily than the phenyl derivatives due to the presence of a longer conjugation chain. The quinones (XII and XIII) are reduced much more easily than the benzoid compounds. Especially important is the fact that the methoxy and acetoxy compounds are reduced at approximately the same $E_{1/2}$ values as the starting compounds (I) and (II). This single fact makes the hydroxy structure (Ia) and (IIa) the most probable for compounds (I) and (II). If these compounds were to represent the betaines (Ic) and (IIc), then their $E_{1/2}$ values should be quite different from the $E_{1/2}$ for the methoxy and acetoxy compounds having a known phenolic structure.

As a result, it is possible to conclude that if 9-hydroxyacridine (IVa) exists only as the oxo compound (acridone) (IVb), then conversely both 9-(p-hydroxyphenyl)acridine (I) and 9-(p-hydroxystyryl)acridine (II) exist only as the hydroxy compounds. In other words, tautomeric transformations are not accomplished through the phenyl ring (or the styryl radical).

The present investigation still does not make it possible to explain the main reason for the absence of tautomeric transformations in the case of compounds (I) and (II). Whether this phenomenon is associated with the presence of the phenyl group or whether it is due to steric hindrance can be answered only by making further studies of the p-hydroxyphenyl derivatives of other N-heterocyclic compounds in which the factor of steric hindrance, characteristic for the 9-phenyl derivatives of acridine, is absent.

Value of the Half Wave Potentials ($E_{1/2}$) for Some Acridine Compounds

Expt. Nos.	Compounds	Value of $E_{1/2}$ (v) with respect to to the normal calomel electrode at pH 8.4	
1	Acridine	−0.700	−1.480
2	9-Methoxyacridine (V)	−0.725	−1.520
3	Acridone (IV)	−	−1.600
4	N-Methylacridone	−	−1.520
5	9-(p-Hydroxyphenyl)acridine (I)	−1.000	−1.345
6	9-(p-Methoxyphenyl)acridine (VI)	−0.940	−1.300
7	9-(p-Acetoxyphenyl)acridine (XI)	−0.950	−1.275
8	9-Phenylacridine (III)	−0.960	−1.290
9	9-(p-Hydroxystyryl)acridine (II)	−0.720	−1.250
10	9-(p-Methoxystyryl)acridine (VII)	−0.800	−1.325
11	9-(p-Acetoxystyryl)acridine	−0.800	−1.290
12	N-Methyl-9-(p-benzoquino)acridan (VIII)	−0.710	−1.320
13	N-Methyl-9-(p-benzoquinoethano)acridan (IX)	−0.405	−1.310

EXPERIMENTAL

1. Synthesis of 9-(p-Hydroxyphenyl)acridine (I). The Landauer method [1] was used to synthesize this compound. Since the purification of this compound by recrystallization is made difficult due to its extremely low solubility in organic solvents, while the high melting point (>340°) does not permit judging as to the purity of the product, then to purify the compound we converted it to the acetyl derivative, which recrystallized well from benzene and had m. p. 212-214°.

Found %: N 4.80. $C_{21}H_{15}O_2N$. Calculated %: N 4.47.

Saponification of the acetyl derivative with dilute acid gave the pure 9-(p-hydroxyphenyl)acridine. Yield 28%.

Found %: N 5.07, 5.40. $C_{19}H_{13}ON$. Calculated %: N 5.16.

2. 9-(p-Methoxyphenyl)acridine (VI). A mixture of 3 g of diphenylamine, 4.25 g of p-methoxybenzoic acid and 9 g of anhydrous $ZnCl_2$ was heated for 4 hours at 210°. The obtained viscous mass was dissolved in 80 ml of boiling alcohol. The hot alcohol solution, dark brown in color, was poured into 200 ml of water, the obtained precipitate was filtered, shaken with 25 ml of concentrated ammonia, again filtered, washed with water, and dried. Then the precipitate was extracted with petroleum ether to removed unreacted diphenylamine. The product was obtained as a pale yellow finely crystalline powder with m. p. 196-201°. Yield 1.76 g (25%). Three recrystallizations from isopropyl alcohol gave 9-(p-methoxyphenyl)-acridine as faintly cream-colored plates with m. p. 211-213° (from [6]: m. p. 213°).

Found %: N 5.15. $C_{20}H_{15}ON$. Calculated %: N 4.91.

The product is readily soluble in acetone, benzene, dioxan and alcohol. In contrast to the hydroxy compound it dissolves in concentrated hydrochloric acid with the formation of an orange-yellow solution.

9-(p-Methoxyphenyl)acridine was also obtained by the methylation of 9-(p-hydroxyphenyl)acridine with dimethyl sulfate in alkaline medium. Yield 86%. M. p. 211-213°.

Found %: C 83.80; H 5.09; N 5.02. $C_{20}H_{15}ON$. Calculated %: C 84.18; H 5.30; N 4.91.

3. N-Methyl-9-(p-benzoquino)acridan (VIII).* a) One gram of 9-(p-acetoxyphenyl)acridine was dissolved in 5 ml of boiling benzene. To the benzene solution was added 1 g of dimethyl sulfate. The reaction mixture was boiled under reflux for 3 hours. Toward the end of heating the deposition of a small amount of yellow-green precipitate was observed; the main portion of the methosulfate deposited from the filtrate on cooling. 9-(p-Acetoxyphenyl)acridine methosulfate was obtained as yellow needles (from methyl alcohol), m. p. 256-260°. Yield 1 g (77%). The product readily dissolves in water to give yellow-green solutions.

b) 9-(p-Acetoxyphenyl)acridine methosulfate (0.7 g) was dissolved in 5 ml of boiling benzene, and to the hot benzene solution was gradually added in drops, with vigorous stirring, 15 ml of water containing 1 ml of concentrated ammonia. A precipitate (fine thin lustrous violet needles) began to deposit immediately in the water layer. The precipitate was filtered, washed well with water, and vacuum-dried at 90°. The product loses some of its luster as the result of drying. M. p. 208-210° (with decompn.). Yield 0.3 g (80%).

Found %: N 4.97. $C_{20}H_{15}ON$. Calculated %: N 4.91.

N-Methyl-9-(p-benzoquino)acridan is very difficultly soluble in nonpolar organic solvents, and somewhat more readily soluble in polar solvents. Its solutions in benzene and dioxan have a crimson color. It dissolves in acetone with a violet color, and in ethyl alcohol with a blue color. It is readily soluble in hydrochloric acid with the formation of a yellow hydrochloride.

4. 9-(p-Hydroxystyryl)acridine (II). A mixture of 3.0 g of p-hydroxybenzaldehyde, 4.8 g of 9-methylacridine and 3.4 g of anhydrous $ZnCl_2$ was heated in an oil bath for 4 hours at 140-145°. The reaction mass melted and began to foam when the temperature reached 135°. Toward the end of the 4-hour heating a hard dark-brown, somewhat viscous melt was formed which was ground, washed well with alcohol, and the obtained brown powder was boiled with 20 ml of alcohol, filtered, and again washed with alcohol. The obtained orange precipitate was boiled with 20 ml of dioxan, which gave a bright yellow powder with m. p. 298-308°.

The 9-(p-hydroxystyryl)acridine was purified through the acetyl derivative, which was obtained as glistening yellow plates (from alcohol) with m. p. 182-183°.

Found %: N 4.44. $C_{23}H_{17}O_2N$. Calculated %: N 4.13.

The saponification of 9-(p-acetoxystyryl)acridine gave fine bright yellow plates of 9-(p-hydroxystyryl)-acridine.

Found %: N 4.88. $C_{21}H_{15}ON$. Calculated %: N 4.71.

5. 9-(p-Methoxystyryl)acridine (VII) was obtained by the same method used to synthesize 9-(p-hydroxystyryl)acridine. From 0.9 g of 9-methylacridine and 0.6 g of p-methoxybenzaldehyde we obtained 0.65 g of 9-(p-methoxystyryl)acridine as fine yellow prisms (from alcohol), m. p. 191-193° (50% yield). The product is readily soluble in alcohol, benzene, acetone, and dioxan, and also in acids with the formation of orange-red solutions. 9-(p-Methoxystyryl)acridine was also obtained by the methylation of 9-(p-hydroxystyryl)acridine. M. p. 191-193°. Yield 72%.

Found %: C 84.57; H 5.64; N 4.38. $C_{22}H_{17}ON$. Calculated %: C 84.86; H 5.50; N 4.50.

6. N-Methyl-9-(p-benzoquinoethano)acridan (IX)** was obtained by the Hunig procedure [4]. From 1 g of 9-methylacridine methosulfate we obtained 0.57 g (61%) of the quinone as thin lustrous dark-purple needles (when heated on the water bath they turn green). M. p. 204-206° (with decompn.).

Found %: N 4.69. $C_{22}H_{17}ON$. Calculated %: N 4.50.

* For indexing purposes the compound can be assigned the following name: 10-methyl-9-(4-oxocyclohexadienylidene)-9,10-acridan.

** 10-Methyl-9-(4-oxocyclohexadienylidene)ethylidene-9,10-acridan.

Polarographic Reduction of the compounds enumerated above was done with the aid of a Geirovsky micropolarograph. For the studies we used solutions with a concentration of $1 \cdot 10^{-3}$. As solvent we took a mixture composed of 75% dioxan and 25% alcohol. All of the measurements were made in ammonia buffer solution with pH 8.4.

SUMMARY

1. Based on a comparison with compounds having an authentic phenolic (VI, VII, X) and an authentic quinoidal (VIII, IX) structure it was established that 9-(p-hydroxyphenyl)acridine (I) and 9-(p-hydroxystyryl)-acridine (II) have the hydroxy structure (Ia, IIa), and neither the oxo nor the betaine structure (Ib, IIb; Ic, IIc). It was postulated that the reason for the weak manifestation of phenolic and basic properties in compounds (I) and (II) is because of the presence of strong intermolecular hydrogen bonds in them.

2. It was shown that the newly synthesized N-methyl-9-(p-benzoquino)acridan (VIII) is an unstable compound. In contrast to N-methyl-9-(p-benzoquinoethano)acridan (IX), it is easily oxidized in the air with the formation of N-methylacridone. This lack of stability is probably associated with a noncoplanar structure.

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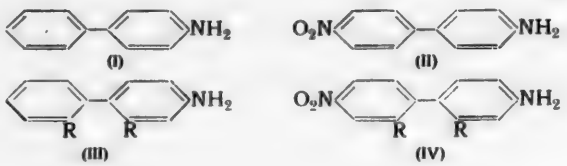
STERIC HINDRANCE AND REACTIVITY

XI. HINDERED INTERNAL ROTATION AND KINETICS OF ACYLATION OF 2,2'-DIMETHOXY AND 3,3'-DIMETHYL DERIVATIVES OF 4-AMINOBIPHENYL AND 4-AMINO-4'-NITROBIPHENYL

L. M. Litvinenko and A. P. Grekov

In previous communications of this series [1-6], as the result of studying the kinetics of the reaction for the acylation of 4-aminobiphenyl (I) and 4-amino-4'-nitrobiphenyl (II), and also the derivatives of these amines containing various 2,2'-substituents (III and IV), we were able to establish that the electronic effect of the NO_2 group on the NH_2 group through the molecular system of biphenyl is noticeably weakened in going from (II) to (IV).



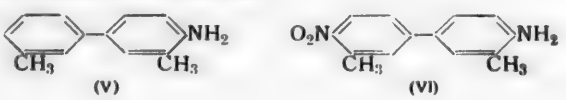
The ratio of the following acylation rate constants:

$$F = \frac{k_I}{k_{II}} : \frac{k_{III}}{k_{IV}}$$

is a convenient measure for quantitatively determining the manner in which the reactivity in the indicated series of compounds changes as a function of variation in the spatial configuration.

The value of F, called by us "the steric factor of weakening the conjugation," shows to what extent interaction of the NO_2 and NH_2 groups found on different sides of the molecular system of biphenyl is diminished due to steric limitations created by the introduction of bulky substituents in the 2,2'-positions of biphenyl.

In order to supplement and expand on the concepts discussed in our previous studies, we give in the present communication the data obtained by us in studying the kinetics of the acylation of some 2,2'-dimethoxy and 3,3'-dimethyl derivatives of (I) and (II) with p-nitrobenzoyl chloride in benzene solution, and specifically of: 4-amino-2,2'-dimethoxybiphenyl (III, R = OCH_3), 4-amino-4'-nitro-2,2'-dimethoxybiphenyl (IV, R = OCH_3), 4-amino-3,3'-dimethylbiphenyl (V) and 4-amino-4'-nitro-3,3'-dimethylbiphenyl (VI). For a more complete comparison of the results obtained in this and previous investigations we also made a study under identical conditions of the kinetics of the acylation of m-anisidine.



The indicated methoxy derivatives are of interest from the viewpoint that the substituent OCH_3, in the value of its van der Waals' radius, is the smallest of the simplest types of groups in the series [7]: $SO_3Na > NO_2 > Cl > CH_3 > COOH > NH_2 > OH > OCH_3$. A study of the reactivity of the 3,3'-dimethyl derivatives of (I) and (II) permits elucidating wherein the effect of 3,3'-substituents on transfer of the electronic interaction of NO_2 and NH_2 groups through the molecular system of biphenyl differs from the effect of 2,2'-substituents, already studied by us quite extensively in analogous cases.

EXPERIMENTAL

Preparation and purification of starting compounds. The benzene and p-nitrobenzoyl chloride were purified in the same manner as indicated in an earlier study [1]. The synthesis and methods of purifying the methox and methyl amino derivatives of biphenyl have been described in a separate communication [8]. m-Anisidine was obtained by the method described in [9] and was first purified as the acetyl derivative by recrystallization from water and alcohol, then as the amine sulfate by several recrystallizations from 10% sulfuric acid, and finally, as the free base by repeated vacuum-distillation.

TABLE 1

Kinetics of the Reaction for the Acylation of 4-Amino-2,2'-dimethoxybiphenyl with p-Nitrobenzoyl Chloride

a 0.00125 mole/liter *b* 0.0025 mole/liter

Temperature 25°				Temperature 50°			
t_1, (min)	yield (%)	k_1, (liter/mole·sec)	n_1	t_1, (min)	yield (%)	k_1, (liter/mole·sec)	n_1
4	25.6	0.576	3	3	37.3	1.37	2
5	29.8	0.570	2	4	43.5	1.39	2
7	38.2	0.592	2	6	52.4	1.27	2
10	46.1	0.573	2	8	60.8	1.34	2
15	56.5	0.581	2	12	70.0	1.34	2
	K_{ss}° 0.578 ± 0.008				K_{ss}° 1.33 ± 0.03		

E 6400 cal/mole PZ $2.8 \cdot 10^4$ l/mole·sec $\Delta S^{\#}$ −40.3 cal/deg.·mole

TABLE 2

Kinetics of the Reaction for the Acylation of 4-Amino-4'-nitro-2,2'-dimethoxybiphenyl with p-Nitrobenzoyl Chloride

a 0.00125 mole/liter *b* 0.0025 mole/liter

Temperature 25°				Temperature 50°			
t_1, (min)	yield (%)	k_1, (liter/mole·sec)	n_1	t_1, (min)	yield (%)	k_1 (liter/mole·sec)	n_1
10	15.2	0.120	2	5	15.8	0.260	2
15	20.6	0.116	2	8	23.0	0.258	2
30	32.2	0.106	2	15	35.7	0.256	2
50	48.4	0.126	3	30	53.2	0.262	3
80	59.9	0.125	3	45	64.0	0.273	3
130	67.6	0.110	2	70	74.3	0.285	2
	K_{ss}° 0.118 ± 0.004				K_{ss}° 0.266 ± 0.007		

E 6200 cal/mole PZ $4.3 \cdot 10^3$ l/mole·sec $\Delta S^{\#}$ −44.0 cal/deg.·mole

TABLE 3

Kinetics of the Reaction for the Acylation of m-Anisidine with p-Nitrobenzoyl Chloride

a 0.00125 mole/liter				b 0.0025 mole/liter			
Temperature 25°				Temperature 50°			
t_i, (min)	yield (%)	k_1, (liter/mole·sec)	n_i	t_i, (min)	yield (%)	k_1, (liter/mole·sec)	n_i
3	16.7	0.447	2	3	31.1	1.04	3
5	24.6	0.437	3	4	36.6	0.998	3
10	39.4	0.435	4	6	45.6	0.963	3
15	48.3	0.417	3	10	62.3	1.14	3
30	66.5	0.443	2	15	70.1	1.08	3
$K_{25°}$ 0.434 ± 0.025				$K_{50°}$ 1.04 ± 0.07			

E 6700 cal/mole; PZ 3.5 · 10^4 l/mole·sec;, $\Delta S^{\#}$ —39.8 cal/deg.·mole

TABLE 4

Kinetics of the Reaction for the Acylation of 4-Amino-3,3'-dimethylbiphenyl with p-Nitrobenzoyl Chloride

a 0.0025 mole/liter				b 0.005 mole/liter			
Temperature 25°				Temperature 50°			
t_i, (min)	yield (%)	k_1, (liter/mole·sec)	n_i	t_i, (min)	yield (%)	k_1, (liter/mole·sec)	n_i
5	19.3	0.158	3	4	34.5	0.455	3
10	32.6	0.162	3	6	44.4	0.459	3
20	49.1	0.162	3	10	56.9	0.458	3
40	65.7	0.161	4	15	67.3	0.474	3
60	74.0	0.159	2	20	73.8	0.486	3
$K_{25°}$ 0.161 ± 0.003				$K_{50°}$ 0.466 ± 0.010			

E 8100 cal/mole; PZ 14.9 · 10^4 l /mole·sec; $\Delta S^{\#}$ —36.9 cal/deg.·mole

TABLE 5

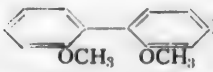
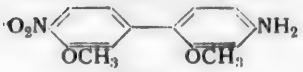
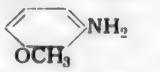
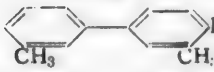
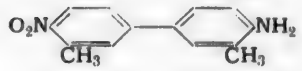
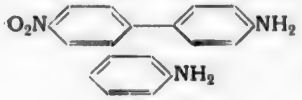
Kinetics of the Reaction for the Acylation of 4-Amino-4'-nitro-3,3'-dimethylbiphenyl with p-Nitrobenzoyl Chloride

a = 0.0025 mole/liter				b = 0.005 mole/liter			
Temperature 25°				Temperature 50°			
t_i, (min)	yield (%)	k_1, (liter/mole·sec)	n_i	t_i, (min)	yield (%)	k_1, (liter/mole·sec)	n_i
20	8.6	0.0158	3	10	13.6	0.0546	2
50	18.5	0.0152	3	25	26.5	0.0498	2
100	30.6	0.0148	3	50	43.2	0.0527	2
180	44.4	0.0149	3	90	57.6	0.0521	3
300	58.4	0.0156	3	150	69.2	0.0517	3
$K_{25°}$ = 0.0153 ± 0.0005				$K_{50°}$ = 0.0521 ± 0.0014			

E = 9400 cal/mole; PZ = 11.6 · 10^4 l/mole·sec; $\Delta S^{\#}$ = —37.4 cal/deg.·mole

TABLE 6

Summary Data on the Kinetics of the Acylation of Amines with p-Nitrobenzoyl Chloride*

Amine	$K_{25}°$	$K_{50}°$	E	PZ	$\Delta S^{\#}$
	0.578 ± 0.008	1.33 ± 0.03	6400	$2.8 \cdot 10^4$	—40.3
	0.118 ± 0.004	0.266 ± 0.007	6200	$4.3 \cdot 10^3$	—44.0
	0.434 ± 0.025	1.04 ± 0.07	6700	$3.5 \cdot 10^4$	—39.8
	0.161 ± 0.003	0.466 ± 0.010	8100	$14.9 \cdot 10^4$	—36.9
	0.0153 ± 0.0005	0.0521 ± 0.0014	9400	$11.6 \cdot 10^4$	—37.4
	0.533 ± 0.010	1.11 ± 0.02	5600	$7.1 \cdot 10^3$	—42.8
	0.0505 ± 0.0011	0.118 ± 0.003	6500	$2.9 \cdot 10^3$	—44.7
	0.580 ± 0.018	—	—	—	—

* The dimensions of the values are the same as those given in Tables 1-5.

Method of measuring the reaction rate and the results. The method used to measure the reaction rate, the techniques used to calculate the kinetic parameters, and an evaluation of their accuracy, have been described in an earlier communication [5].

In all of the experiments the initial concentration of the acid halide (a) was always exactly half of the initial concentration of the amine (b).

The numerical data obtained for the reactions investigated in the present study are collected in Tables 1-5, where the following designations hold: t_i is the total elapsed time between measurements of the rate; k_i and K are respectively the average values of the rate constants: 1) for a given t_i with the number of measurements equal to n_i, and 2) for all of the Σn_i measurements, E is the energy of activation; PZ is the frequency factor; and $\Delta S^{\#}$ is the entropy of activation. In Tables 1-5 the average values of the reaction yield for the n_i measurements are given in the second column.

The principal data on the kinetics of the reactions investigated by us in the present study are summarized in Table 6, as are also some of the values for the reactions studied by us earlier [2, 5].

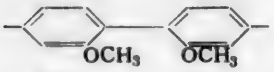
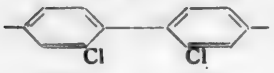
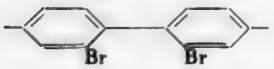
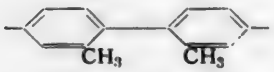
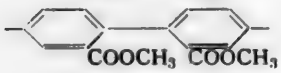
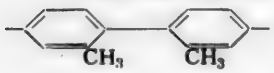
DISCUSSION OF RESULTS

The experimental results, collected in Table 6, reveal that a meta-methoxy group manifests a slight electron-acceptor effect, since the rate constant decreases somewhat in the transition from aniline to m-anisidine. The fact that the acylation rates of 4-aminobiphenyl and its dimethoxy derivative are nearly the same is evidence that in this case the total effect of two methoxy groups on the reactivity of an amino group, connected to the biphenyl radical, either in general bears an electroneutral character or even has a very weakly expressed electron-donor nature. This can be explained only by assuming that the two methoxy groups exert an opposite influence on the amino group: one of then is an acceptor (2-position), and the other is a donor (2'-position) of electrons. The mentioned observation is in good agreement with the known fact that a meta-methoxy group possesses electron-acceptor properties, while a para-methoxy group possesses electron-donor properties [10].

If the introduction of two methoxy groups in the 2 and 2' positions of the 4-aminobiphenyl molecule is practically without effect on the reactivity of the latter, then in the case of the analogous 4'-nitro derivatives we observe a different situation: the acylation rate constant more than doubles in the transition from 4-amino-4'-nitrobiphenyl to 4-amino-4'-nitro-2,2'-dimethoxybiphenyl. Taking into consideration what has been said above relative to the mutual action of the two methoxy groups, this increase in the rate must be regarded as being entirely due to the steric hindrance exerted by the indicated groups, which facilitates a weakening of the conjugation between the benzene rings in the molecular system of biphenyl, and consequently causes some reduction in the influence exerted by the 4'-nitro group on the 4-amino group through the given system. A quantitative estimate of such a steric effect can be obtained with the aid of factor F, mention of which was made at the start.

TABLE 7

Values of the F Factors for the Molecular Systems of Biphenyl and Some of Its 2,2'-Disubstituted Derivatives

System	$F_{25°}$	$F_{50°}$
	1.00	1.00
	2.11	1.88
	1.65	1.76
	1.73	1.80
	1.52	2.03
	2.71	2.67
	1.00	1.05

The values of this term for the biphenyl system with various 2,2'-substituents are collected in Table 7. It can be seen from the presented data that despite their small size the methoxy groups manifest a steric effect that in magnitude is not different from the effect caused by more bulky substituents in the 2,2'-positions of the 4-amino-4'-nitrobiphenyl molecule.

The effect of introducing methyl groups in the 3,3'-positions on the reactivity of 4-aminobiphenyl consists in a substantial reduction of the acylation rate for the latter. This is in agreement with the fact that a methyl group in the ortho-position to an amino group, due to the so-called ortho-effect, is responsible for a decrease in the acylation rate of aromatic amines [11]. Here the electron-donor influence of a methyl group found in the second benzene ring (2'-position), with exertion of the influence through the internuclear bond, cannot be taken into consideration [4].

The data in the same Table 7 also show that the introduction of methyl groups in the 3,3'-positions of the 4-amino-4'-nitrobiphenyl molecule, in contrast to the analogous 2,2'-substituents, does not lead to a weakening of the interaction between the NO_2 and NH_2 groups: the value of the F factor for the 3,3'-disubstituted biphenyl system, the same as for the molecular system of unsubstituted biphenyl itself, is equal to unity. As a result 3,3'-substituents, in contradistinction to 2,2'-substituents, exert very little influence on the conductivity

of the molecular system of biphenyl relative to the electronic interferences exerted by groups located in the 4,4'-positions. However, one of the 3,3'-substituents in the discussed case being found in direct proximity to the amino group, due to the screening effect [12], causes a decrease in the activity of the latter.

A difference in the character of the action of 2,2'- and 3,3'-substituents can be explained most readily by stating that the latter, in contrast to the former, should not cause an increase in the angle between the planes of the benzene rings in the molecules of biphenyl and its derivatives, and consequently a weakening of the conjugation between the two rings. Measurements by the electronographic method [13] of similar angles in the series comprising the simplest 2,2'- and 3,3'-disubstituted derivatives of biphenyl actually confirms such a viewpoint. The results obtained in the present study are also in complete accord with the conclusions derived on the basis of making a comparative study of the absorption spectra of biphenyl derivatives of the indicated structure [7, 14], and they are also in accord with the conclusions derived in the investigations made recently in our laboratory by Krasovitsky and Pereyaslova, and directed toward an elucidation of the rules governing color and certain other properties of the azo dyes obtained from benzidine derivatives with various substituents in the 2,2'- and 3,3'-positions.

From the viewpoint of energy characteristics the reactions investigated in the present study can be characterized by saying that of the two pairs of disubstituted biphenyl derivatives studied, the dimethoxy amino derivatives are characterized by somewhat smaller values of the energy and of the entropy of activation. In connection with the fact that 2,2'-dimethoxy groups exert by the electronic mechanism an even smaller influence on the reactivity of the 4-amino group than do the 2,2'-dimethyl groups in a like case, we were justified in expecting, by analogy with the data obtained in our previous studies [1, 2, 4], an increase in the values of E and $\Delta S^{\#}$ in going from 4-amino-4'-nitrobiphenyl to its 2,2'-dimethoxy derivative. However, this was not confirmed by experiment. It is possible that the fact that the volume dimensions of methoxy groups are much smaller than they are for methyl groups is responsible for specifically this difference in the influence exerted by 2,2'-dimethyl and 2,2'-dimethoxy groups on the peculiar variation of E and $\Delta S^{\#}$ in the examined series of compounds.

SUMMARY

1. In order to elucidate the relationship between spatial structure and reactivity in the series of amino derivatives of biphenyl we studied the kinetics of the acylation of 4-amino-2,2'-dimethoxybiphenyl, 4-amino-4'-nitro-2,2'-dimethoxybiphenyl, m-anisidine, 4-amino-3,3'-dimethylbiphenyl and 4-amino-4'-nitro-3,3'-dimethylbiphenyl with p-nitrobenzoyl chloride in benzene solution.

2. It was shown that a transfer of the electronic interaction between NO_2 and NH_2 groups (in the 4 and 4' positions) through the molecular system of biphenyl is weakened when 2,2'-dimethoxy substituents are introduced due to the steric hindrance that is created in this connection, leading to a change in the geometric configuration of the biphenyl molecule. However, the indicated interaction remains unchanged in going from the molecular system of unsubstituted biphenyl to the biphenyl system containing 3,3'-substituents. This is explained by the fact that 3,3'-substituents exert very little influence on the internal rotations of the benzene rings in the molecules of biphenyl and its derivatives.

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REACTIONS OF HYDRAZINE DERIVATIVES

XVI. THE ACTION OF BENZYL CHLORIDE ON ACYLHYDRAZONES

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Acylhydrazones are easily enolized, while the metallic derivatives of these enols are capable of alkylation with transfer of the reaction center to the nitrogen atom. Thus, the lead enolate of N,N'-diformylhydrazine when reacted with alkyl halides is converted into the N,N'-dialkyl-N,N'-diformylhydrazine, from which sym-dialkylhydrazines [1] can be obtained by hydrolysis. In a similar manner N,N'-dibenzoylhydrazine readily forms the sodium enolate, which when reacted with benzyl chloride is converted to N,N'-dibenzoylbenzylhydrazine, extremely stable to hydrolysis [2].

In one of our previous communications [3] we described the synthesis of benzylhydrazine, based on the conversion of the acetylhydrazone of acetone (I) into the sodium enolate (II), with subsequent reaction with benzyl chloride and then hydrolysis. This synthesis was subjected to a more systematic study in the present investigation.

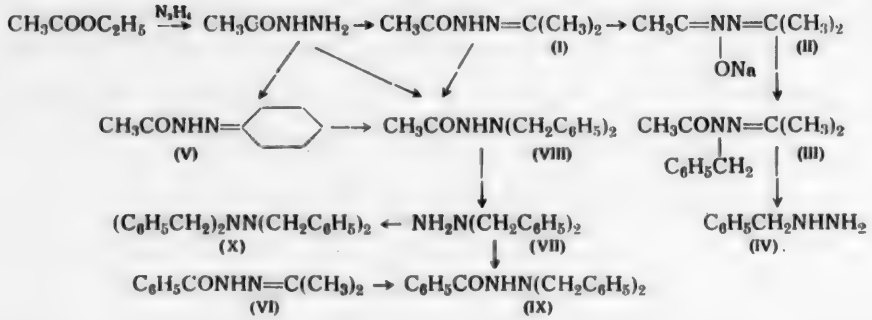
Running the process under mild conditions to avoid hydrolysis, we isolated the intermediate reaction product—the acetylbenzylhydrazone of acetone (III), which is easily hydrolyzed (with the cleavage of acetic acid and acetone) to yield benzylhydrazine (IV). When the reaction is run under more drastic conditions (prolonged heating with excess benzyl chloride) the yield of benzylhydrazine is reduced and a certain amount (9-20%) of sym-dibenzylhydrazine is formed.

If not the sodium enolate is taken for benzylation, but instead a mixture of hydrazone (I) with either triethylamine or pyridine, then benzylation does not take place in the absence of water (the chlorobenzylate of the corresponding amine was isolated instead), The reaction proceeds very easily in the presence of water and leads to a substance with m. p. 108°.

To determine the structure of this substance we benzylated the acetylhydrazone of cyclohexanone (V) and the benzylhydrazone of acetone (VI). In the first case we obtained a substance with m. p. 108°, identical with the above mentioned, and in the second case we obtained a substance with m. p. 165°. The action of benzyl chloride on acetylhydrazine also gave a substance with m. p. 108°. Acid hydrolysis of this substance gave the hydrochloride of unsym-dibenzylhydrazine (VIII) in quantitative yield. This conclusively elucidates the structure of the obtained compounds. The substance with m. p. 108° is the acetyl derivative of unsym-dibenzylhydrazine (VIII), while the substance with m. p. 165° is the benzoyl derivative (IX). The last compound was also obtained by the benzoylation of unsym-dibenzylhydrazine (VII) by the Schotten-Baumann reaction.

As a result, acylhydrazones as the sodium enolates, in anhydrous medium attach the benzyl radical to the same nitrogen atom as contains the acyl group, while under drastic conditions the second benzyl radical adds to the second nitrogen atom. In aqueous media a molecule of the ketone is readily cleaved, and the formed acylhydrazine is now benzylated not at the amido, but instead at the amino group of the hydrazine.

The yield of acyl-unsym-dibenzylhydrazine depends on the strength of the base that is used, which combines with the hydrogen chloride liberated during reaction. If in the presence of pyridine the yield of N'-acetyl-N,N-dibenzylhydrazine (VIII) from hydrazone (I) was only 14%, then with triethylamine the yield rose to 50%. The maximum yield (70%) was obtained by the benzylation of acetylhydrazine in the presence of triethylamine.



It should be mentioned that when benzyl chloride was reacted with acetylhydrazine in aqueous soda solution the main reaction product proved to be tetrabenzylhydrazine (X), i.e., the acetyl group is also cleaved under these conditions.

Extension of the described reactions to other alkyl halides might be of interest for the synthesis of unsymdialkylhydrazines.

EXPERIMENTAL

Acetylhydrazine. To a mixture of 260 g of 96% hydrazine hydrate and 100 ml of ethyl alcohol was added at the boil 480 g of ethyl acetate in 3 hours. After this the heating was continued for another 4 hours, the mixture allowed to stand overnight, and then the alcohol and water were removed by distillation under reduced pressure on the water bath. Vacuum-distillation of the residue gave 295 g (80%) of acetylhydrazine with b. p. 122-145° at 18 mm. After redistillation, b. p. 129-131° at 18 mm, and m. p. 65° (from alcohol). Literature: b. p. 129° at 18 mm [4], and m. p. 67° [5].

The residue after distilling off the acetylhydrazine was also vacuum-distilled to give 85 g (11.6%) of N,N'-diacetylhydrazine with b. p. 189-192° at 6 mm, and m. p. 135° (from anhydrous alcohol). Literature: b. p. 209° at 15 mm, and m. p. 138° [6].

Acetone acetylhydrazone (I). To a solution of 37 g of acetylhydrazine in 25 ml of alcohol was rapidly added with stirring 40 ml of pure acetone. The alcohol and excess acetone were evaporated on the water bath, while the residue was dried at 100°. The yield was quantitative, m. p. 137° (from alcohol). Literature: m. p. 133° [5], 136° [7].

The sodium enolate of acetone acetylhydrazone (II) was obtained by dissolving 74 g of acetylhydrazine in 600 ml of pure acetone. To the solution with stirring was gradually added a solution of 40 g of NaOH in 50 ml of water. After heating for 10 minutes on the water bath the mixture was cooled and the crystals filtered on a Buchner funnel. After washing with acetone and absolute ether the substance was dried at 100°, then ground to a fine powder, and dried further in a vacuum oven at the same temperature. Yield 95%. The sodium enolate was prepared in the same manner from the finished acetone acetylhydrazine (I) in quantitative yield.

Acetone acetylbenzylhydrazone (III). A mixture of 27.2 g of the sodium enolate of acetone acetylhydrazone (II) and 28 g of benzyl chloride was heated for 30 minutes in an oil bath at 150-160°. After cooling, 40 ml of benzene was added and the sodium chloride was separated. The filtrate was washed twice with water, and then dried over fused potash. The benzene was distilled off on a water bath, and the residue was vacuum-distilled. We obtained 17 g (41.7%) of acetone acetylbenzylhydrazone (III) with b. p. 140-150° at 4 mm. After three distillations the substance had b. p. 140-141° at 3 mm, n_D^{20} 1.5378, d_4^{20} 1.0522, MR_D 60.71; calc. 60.88.

Found %: C 70.34, 70.46; H 7.76, 7.81. $C_{12}H_{16}ON_2$. Calculated %: C 70.57; H 7.88.

A mixture of 1 g of (III) and 6 ml of concentrated hydrochloric acid was evaporated. The sirupy mass obtained toward the end was treated with 10 ml of concentrated hydrochloric acid and the obtained crystals were separated. We obtained 0.8 g of benzylhydrazine (IV) hydrochloride. The yield was quantitative, m. p. 110° (from alcohol). Literature: m. p. 110° [8].

To obtain benzylhydrazine without isolating (III), we heated 27.2 g of the sodium enolate (II) with 38 g of benzyl chloride at the boil for 40 minutes. After separating the sodium chloride the mixture was evaporated with 150 ml of concentrated hydrochloric acid to dryness. The residue was dissolved in 150 ml of boiling anhydrous alcohol and the hydrazine hydrochloride was separated. Cooling of the filtrate gave 3.2 g (9%) of sym-dibenzylhydrazine hydrochloride with m. p. 218° (decompn.). Literature: m. p. 225° [9].

Found %: N 11.53, 11.74. $C_{14}H_{17}N_2Cl$. Calculated %: N 11.29.

The substance does not give a hydrazone with either benzaldehyde or acetone. The dibenzoyl derivative has m. p. 162° [9].

Evaporation of the filtrate to a volume of 50 ml, followed by the addition of 200 ml of ether, gave 22.5 g (70%) of benzylhydrazine hydrochloride with m. p. 109°.

When the time of heating was increased to 80 minutes the yield of benzylhydrazine dropped to 45%, and that of the sym-dibenzylhydrazine increased to 20%. The heating of an equimolar mixture of (II) with benzyl chloride in an oil bath for 30 minutes at 140-150° gave only benzylhydrazine (78% yield).

Action of benzyl chloride on acetone acetylhydrazone. A mixture of 11.4 g of acetone acetylhydrazone, 28 g of benzyl chloride, 22.4 g of triethylamine and 10 ml of water was boiled for 50 minutes. The reaction mixture was treated with 200 ml of water and then cooled. The viscous oil that separated here soon crystallized. The filtrate was removed by suction-filtration, and the crystals were washed with water and dried at 90°. We obtained 12.8 g (50%) of N'-acetyl-N,N -dibenzylhydrazine (VIII) with m. p. 108° (from 60% alcohol).

Found %: C 76.19, 76.02; H 7.35, 7.46; N 11.09, 11.12. $C_{16}H_{18}ON_2$. Calculated %: C 75.56; H 7.13; N 11.02.

The picrate has m. p. 135° (from benzene).

Found %: N 14.54, 14.70. $C_{22}H_{21}O_8N_5$. Calculated %: N 14.49.

Replacement of the triethylamine by pyridine reduced the yield of (VIII) to 14%. The reaction does not go under anhydrous conditions. (The starting hydrazone and triethylamine chlorobenzylate were isolated instead.)

Action of benzyl chloride on cyclohexanone acetylhydrazone. Cyclohexanone acetylhydrazone (V) was obtained by the evaporation of equimolar amounts of acetylhydrazine and cyclohexanone in alcohol solution. The yield was quantitative, m. p. 124° (from alcohol).

Found %: N 18.28, 18.45. $C_8H_{14}ON_2$. Calculated %: N 18.16.

A mixture of 7.7 g of (V), 14 g of benzyl chloride, 11.2 g of triethylamine and 20 ml of water was boiled for 40 minutes under reflux and then steam-distilled (the distillate contained cyclohexanone, which formed a separate layer). Cooling of the solution that remained in the flask gave 4.6 g (VIII) with m. p. 108° (from dilute alcohol). Yield 36%. The substance fails to depress the melting point when mixed with the substance obtained from acetone acetylhydrazone.

Hydrolysis of N'-acetyl-N,N-dibenzylhydrazine. A mixture of 10 g of (VIII) and 200 ml of dilute (1:1) hydrochloric acid was heated under reflux for 10 hours. The solution was evaporated to dryness and gave 9.8 g of N,N-dibenzylhydrazine (VII) hydrochloride. The yield was quantitative, m. p. 197° (from alcohol). Literature: m. p. 200° [10].

Benzoyl derivative: m. p. 165° (from alcohol). Literature: m. p. 166-168° [11].

Benzaldehyde dibenzylhydrazone was obtained from benzaldehyde and (VII) in the presence of acetate buffer. The yield was quantitative, m. p. 83° (from alcohol). Literature: m. p. 85° [12].

Action of benzyl chloride on acetone benzoylhydrazone. Acetone benzoylhydrazone was obtained by dissolving 65.5 g of benzoylhydrazine in 150 ml of pure acetone. To the solution after cooling was added 40 ml of ether, and the crystals were separated, washed with ether, and dried. Yield 82%, m. p. 144°. Literature: m. p. 142° [13].

A mixture of 16 g of acetone benzoylhydrazone, 28 g of benzyl chloride, 22.4 g of triethylamine and 60 ml of water was boiled for 1 hour, the mixture diluted with water to a volume of 1 liter, and the liquid removed by suction-filtration. Drying of the precipitate gave 12 g (38%) of N'-benzoyl-N,N-dibenzylhydrazine (IX) with m. p. 166° (from alcohol). The substance does not depress the melting point when mixed with the substance obtained by the benzoylation of (VII) by the Schotten-Baumann method.

Found %: C 79.35, 79.51; H 6.61, 6.62. $C_{21}H_{20}ON_2$. Calculated %: C 79.71; H 6.37.

Action of benzyl chloride on acetylhydrazine. A mixture of 7.4 g of acetylhydrazine, 28 g of benzyl chloride, 22.4 g of triethylamine and 10 ml of water was boiled for 45 minutes, then treated with 100 ml of water, and cooled. The crystals were separated, washed with water, and dried. We obtained 18 g (70%) of acetyldibenzylhydrazine (VIII) with m. p. 108° (from dilute alcohol).

The reaction does not proceed as smoothly under anhydrous conditions, and the yield of (VIII) drops to 42%.

The boiling of 7.4 g of acetylhydrazine, 28 g of benzyl chloride and 57 g of crystalline soda in 60 ml of water gave an oily layer which partially crystallized on standing in the cold. The oil was separated and diluted with alcohol to give 6 g (30%) of tetrabenzylhydrazine (X) with m. p. 138° (from alcohol). Literature: m. p. 139.5° [14].

Found %: N 7.25, 7.26. $C_{28}H_{28}N_2$. Calculated %: N 7.14.

SUMMARY

1. Depending on the conditions, the reaction of acetone acetylhydrazone with benzyl chloride gives (after hydrolysis) benzylhydrazine and either symmetrical or unsymmetrical dibenzylhydrazine.

2. The reaction of benzyl chloride with acetylhydrazine can serve as a method for the preparation of unsym-dibenzylhydrazine.

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REACTIONS OF HYDRAZINE DERIVATIVES

XVII. NEW SYNTHESIS OF α-METHYLTRYPTOPHOL

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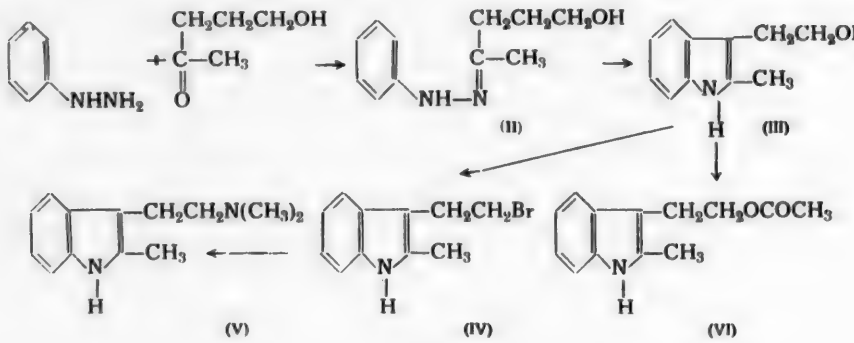
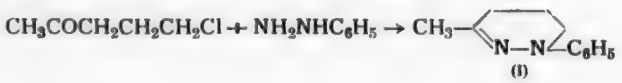
In 1889 Lipp [1] reported that 1-phenyl-3-methyl-1,4,5,6-tetrahydropyridazine (I) is very easily obtained by the reaction of phenylhydrazine with acetopropyl alcohol. In attempting to reproduce Lipp's experiments we obtained a substance with the constants indicated by him, but it proved to be not the tetrahydropyridazine (I), but instead the uncyclized phenylhydrazone of acetopropyl alcohol (II). This phenylhydrazone (II) easily cleaves phenylhydrazine when treated with either hydrochloric acid or benzaldehyde. When heated to 200° it does not cleave water and does not migrate into the tetrahydropyridazine (I), but in the presence of catalytic amounts of zinc chloride or cuprous chloride it is easily converted into α-methyltryptophol (III), in which connection the presence of the isomeric 2-(3-hydroxypropyl)indole as impurity could not be shown. The structure of α-methyltryptophol (III) was confirmed by its conversion through the bromide (IV) into the substituted tryptamine, and specifically into 2-methyl-3-dimethylaminoethylindole (V).

The described combination of reactions not only confirms the structure of the phenylhydrazone (II), but is also a new route for the preparation of α-methyltryptophol (III), which up to now has been obtained by the reduction of the esters of α-methyl-β-indoleacetic acid [2], a much more complicated process.

α-Methyltryptophol (III) when treated with acetic anhydride is easily converted into the acetate (VI), which was characterized as the picrate.



It should be mentioned that by reacting phenylhydrazine with methyl γ-chloropropyl ketone we nevertheless were able to synthesize the pyridazine (I), which proved to be stable toward hydrochloric acid, and did not react with benzaldehyde at room temperature. It remains unchanged when heated with traces of zinc chloride, while with an equimolar amount of the latter complete tarring occurred (we were unable to isolate 1,2-trimethyleneindole).



In contrast to the phenylhydrazone (II), our pyridazine (I) readily gives the picrate.

EXPERIMENTAL

Acetopropyl alcohol phenylhydrazone (II). A mixture of 10.8 g of phenylhydrazine, 10.2 g of acetopropyl alcohol and 6 ml of glacial acetic acid was heated on the water bath for 30 minutes at 80-100°. The reaction mass was made alkaline with ammonia and the separated oil was extracted with ether. The ether extract was dried over potash and then vacuum-distilled. We obtained 17 g (88.5%) of the phenylhydrazone (II) as an extremely viscous oil with b. p. 194-196° (8 mm).

Found %: C 68.60, 68.75; H 8.34, 8.47. $C_{11}H_{16}ON_2$. Calculated %: C 68.71; H 8.38.

On prolonged standing the hydrazone (II) crystallized to a yellow mass with m. p. 60-66°. It does not give a picrate. It is hydrolyzed by concentrated hydrochloric acid to phenylhydrazine hydrochloride, and with benzaldehyde it gives the phenylhydrazone of benzaldehyde. It rapidly oxidizes in the air, but stores well in sealed ampuls.

Acetopropyl alcohol phenylhydrazone (II) can be obtained in a completely similar manner by mixing equimolar amounts of phenylhydrazine and acetopropyl alcohol and heating them on the water bath in the absence of acetic acid; yield 90%.

1-Phenyl-3-methyl-1,4,5,6-tetrahydropyridazine (I). A solution of 51 g of methyl γ-chloropropyl ketone in 50 ml of alcohol and 48.6 g of phenylhydrazine were mixed in a flask fitted with a Dimroth reflux condenser. On conclusion of exothermic reaction the mixture was heated for 1 hour on the water bath, then about 40 ml of alcohol was distilled off, the remainder made alkaline with ammonia, and the separated oil extracted with ether. The ether extract after drying over potash was vacuum-distilled. We obtained 41 g (52.4%) of the pyridazine (I) with b. p. 197-198° (6 mm) as an extremely viscous oil that failed to crystallize even after standing for a month, and did not oxidize when exposed to the air.

Found %: N 16.09, 16.18. $C_{11}H_{14}N_2$. Calculated %: N 16.07.

An alcohol solution of the pyridazine (I) when mixed with picric acid gave the picrate as a fine yellow powder, difficultly soluble in alcohol, and with m. p. 226.5° (from alcohol).

Found %: N 17.20, 17.24. $C_{11}H_{14}N_2 \cdot C_6H_3O_7N_3$. Calculated %: N 17.36.

α-Methyltryptophol (III). A mixture of 15.7 g of phenylhydrazine and 15.3 g of acetopropyl alcohol in a 50 ml Claisen flask was heated on the water bath for 1 hour and then the water was distilled off under the vacuum of a water-jet pump until the temperature of the mixture reached 150°. The sirupy acetopropyl alcohol phenylhydrazone (II) obtained here was treated with 0.2 g of cuprous chloride and then heated in a metal bath. A copious evolution of ammonia began at 190° and an exothermic reaction set in, in which connection the temperature rose to 230°. Heating was continued for 2 hours at 210°, after which the reaction mixture was vacuum-distilled. We obtained 15.6 g (69.4%) of α-methyltryptophol with b. p. 202-204° (7-8 mm) as viscous oil, which crystallized after prolonged cooling to a crystalline mass with m. p. 52-55°.

A mixture of 3.5 g of α-methyltryptophol and 4.6 g of picric acid was heated in 25 ml of alcohol. On cooling, the picrate precipitated as extremely fine bright-red fibrils with m. p. 132° (from alcohol).

Found %: N 13.62, 13.65. $C_{11}H_{13}ON \cdot C_6H_3O_7N_3$. Calculated %: N 13.85.

Literature [2]: b. p. 198° (3.5 mm), m. p. 55-56°. Picrate, m. p. 134.5° (from alcohol).

α-Methyltryptophol (III) can also be obtained in 63% yield by heating acetopropyl alcohol phenylhydrazone (II) with catalytic amounts of anhydrous zinc chloride.

O-Acetyl-α-methyltryptophol (VI). To a solution of 94 g of crude acetopropyl alcohol phenylhydrazone (II) in a mixture of 150 ml of dioxan and 150 ml of carbon tetrachloride was added 200 ml of acetyl chloride in drops. On conclusion of exothermic reaction the ammonium chloride was filtered, the solvent was distilled off in vacuo, and the residue was fractionally distilled. We obtained 26 g (33.4%) of O-acetyl-α-methyltryptophol (VI) with b. p. 196-204° (3-4 mm).

The picrate, obtained as dark purple crystals, has m. p. 131.5° (from alcohol).

Found %: C 51.35, 51.31; H 4.20, 4.21. $C_{13}H_{15}O_2N \cdot C_6H_3O_7N_3$. Calculated %: C 51.12; H 4.08.

O-Acetyl-α-methyltryptophol can also be obtained by boiling α-methyltryptophol (III) with a 4-fold amount of acetic anhydride. The yield was quantitative. Picrate, m. p. 131.5°; the melting point is not depressed when this picrate is mixed with the picrate obtained above. A mixture of this picrate with the picrate of α-methyltryptophol (m. p. 132°) gives a melting point depression of 25°.

α-Methyl-β-(β'-bromoethyl)indole (IV). To a solution of 20 g of α-methyltryptophol in 350 ml of absolute ether was slowly added in drops a solution of 20 g of phosphorus tribromide in 50 ml of absolute ether, after which the mixture was allowed to stand overnight. The ether was decanted, washed with water, then with soda solution, again with water, dried over anhydrous magnesium sulfate, and the ether distilled off. We obtained 19.1 g (70.3%) of α-methyl-β-(β'-bromoethyl)indole as yellow crystals with m. p. 58°.

Found %: N 5.64, 5.80. $C_{11}H_{12}NBr$. Calculated %: N 5.88.

α-Methyl-β-(β'-dimethylaminoethyl)indole (V). A mixture of 4.8 g of α-methyl-β-(β'-bromoethyl)-indole (IV), 15 ml of 33% aqueous dimethylamine solution and 15 ml of methyl alcohol was heated in a sealed ampul at 100° for 10 hours. The reaction mass was poured into an excess of dilute hydrochloric acid and the neutral reaction products were removed by extraction with ether. The water extract was made alkaline, and the separated tryptamine was extracted with ether. The ether extract was dried over magnesium sulfate and then vacuum-distilled. We obtained 2.7 g (66.5%) of α-methyl-β-(β'-dimethylaminoethyl)indole (V) with b. p. 204-205° (21 mm). The substance is a viscous yellow oil with an unpleasant odor, and slowly crystallizes on standing. M. p. 93-95° (from alcohol).

The picrate was obtained as a fine orange powder with m. p. 176° (from alcohol).

Found %: C 52.91, 52.82; H 5.14, 5.02. $C_{13}H_{18}N_2 \cdot C_6H_3O_7N_3$. Calculated %: C 52.89; H 4.92.

Literature data: distills in a vacuum of 4.5 mm at a bath temperature of 180-184°; m. p. 97-98°; picrate, m. p. 174-175° [2].

SUMMARY

The reaction of acetopropyl alcohol with phenylhydrazine was studied. A new method for the preparation of α-methyltryptophol was proposed.

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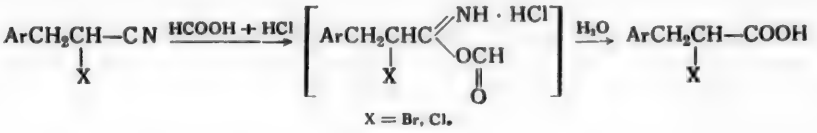
HALOARYLATION OF UNSATURATED COMPOUNDS BY AROMATIC DIAZO COMPOUNDS

IX. SYNTHESIS OF α-HALO-β-ARYLPROPIONIC AND β-ARYLISOBUTYRIC ACIDS

A. B. Dombrovsky, A. M. Yurkevich and A. P. Terentyev

Studying the possibility of the direct synthesis of phenylalanine and its derivatives by the haloarylation of acrylonitrile [1], we developed a method for the preparation of α-halo-β-arylpropionic acids by the hydrolysis of α-halo-β-arylpropionitriles with a mixture of formic and hydrochloric acids. The single known satisfactory method for the synthesis of α-halo-β-arylpropionic acids consists in the treatment of phenylalanine or its aryl derivatives with nitrous acid and hydrochloric acid or potassium bromide [2, 3], but this method cannot be used for the synthesis of amino acids. Attempts to hydrolyze α-halo-β-arylpropionitriles with 20% hydrochloric acid led to obtaining small amounts of halo acids mixed with substituted cinnamic acids [4, 5]. Our experiments on the hydrolysis of chloronitriles in glacial acetic and trichloroacetic acids also gave low yields of the corresponding acids.

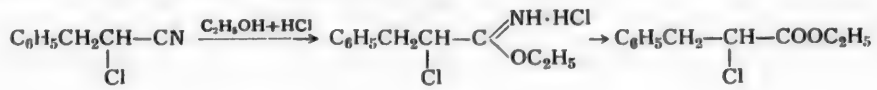
The method proposed by us for the hydrolysis of α-halo-β-arylpropionitriles with a mixture of formic and hydrochloric acids leads to the rapid formation of the corresponding α-halo acids in yields that are close to quantitative. The heating of the chloronitrile was run with a 3-5-fold amount of 85% formic and concentrated hydrochloric acids. The following acids were obtained with this method: α-chloro-β-phenyl- (I), α-chloro-β-(p-methoxyphenyl)- (II), α-chloro-β-(p-chlorophenyl)- (III), α-chloro-β-(2,4-dichlorophenyl)- (IV), α-chloro-β-(p-bromophenyl)- (V), α-chloro-β-(p-nitrophenyl)- (VI) and α-bromo-β-phenylpropionic (VII) acids.



X = Br, Cl.

Under similar conditions we obtained α-chloro-β-phenyl- (VIII) and α-chloro-β-(p-nitrophenyl)-isobutyric (IX) acids from the corresponding methyl esters. In addition, acid (VIII) was obtained by the haloarylation of methacrylic acid (X) with phenyldiazonium chloride.

The special role played by formic acid in this process is apparently due to its participation in the formation of the intermediate product—the hydrochloride of the imino anhydride, which is then saponified to the acid. The ability of the nitrile group to participate in addition reactions was shown by us on the example of the reaction of α-chloro-β-phenylpropionitrile (XI) with alcoholic HCl solution; here the imino ester hydrochloride of acid (I) was obtained—an unstable compound which is rapidly converted by traces of moisture into the ethyl ester of α-chloro-β-phenylpropionic acid.



The presence of a halogen atom in the α-position probably facilitates the addition of a molecule of alcohol or of formic acid to the nitrile group, similar to the case of α-chloro-β-phenylpropionaldehyde where the α-halogen atom favors the addition of water and of alcohol, respectively leading to the formation of the hydrate and acetal of this aldehyde [6].

EXPERIMENTAL

α-Chloro-β-phenylpropionic acid (I). To 7.7 g of (XI) in a flask fitted with reflux condenser was added a mixture of 15 ml of 85% formic acid and 10 ml of concentrated hydrochloric acid.. After heating for 10 hours the reaction mixture was diluted with water (20 ml). (I) deposited from the solution on cooling. Recrystallization from alcohol gave 8.3 g (96.5%) of colorless plates with m. p. 49-50° (from water). The L-isomer of (I) with b. p. 176-177° at 20 mm is described in the literature [2].

Found %: C 58.25, 58.14; H 4.96, 4.97; Cl 19.10, 19.23. $C_9H_9O_2Cl$. Calculated %: C 58.55; H 4.91; Cl 19.21.

α-Chloro-β-(p-methoxyphenyl)propionic acid (II). From 9.45 g of α-chloro-β-(p-methoxyphenyl)propionitrile synthesized by the method described in one of our previous communications [1], after treatment in the same manner as described above (12 ml of 85% formic acid and 5 ml of concentrated hydrochloric acid, 15 hours), we obtained 4.15 g (40%) of acid (II) as a colorless noncrystallizing sirup with b. p. 187-189° at 7 mm.

Found %: M 214, 192 (NaOH titration). $C_{10}H_{11}O_3Cl$. Calculated %: M 214.6.

α-Chloro-β-(p-chlorophenyl)propionic acid (III). From 9.15 g of α-chloro-β-(p-chlorophenyl)propionitrile, obtained from acrylonitrile and diazotized p-chloroaniline [1], we isolated after hydrolysis 9.8 g of (III). Yield 97%. White crystals with m. p. 98-99° (from aqueous alcohol). Literature data: m. p. 98-100° [5].

α-Chloro-β-(2,4-dichlorophenyl)propionic acid (IV). α-Chloro-β-(2,4-dichlorophenyl)propionitrile [1] (7.2 g) was treated with a mixture of 15 ml of 85% formic acid and 10 ml of concentrated hydrochloric acid (heating for 12 hours). (IV) was obtained as needlelike crystals. Weight 6.15 g (79%), m. p. 145-146° (from water).

Found %: C 42.89, 42.75; H 2.94, 2.97. $C_9H_7O_2Cl_3$. Calculated %: C 42.64; H 2.78.

α-Chloro-β-(p-bromophenyl)propionitrile (XII). A solution of p-bromophenyldiazonium chloride was prepared from 34.8 g of p-bromoaniline and added to a solution of 10.5 g of acrylonitrile in 100 ml of acetone. Nitrogen began to evolve (18-25°) after the addition of 5 g of cupric chloride and 4 g of magnesium oxide. After the usual treatment of the reaction mixture [1] we obtained 36.5 g of α-chloro-β-(p-bromophenyl)propionitrile (XII) as a yellow oil with b. p. 154-155.5° at 6 mm.

n_D^{20} 1.5729, d_4^{20} 1.602, MR_D 50.03; calc. 52.61.

Found %: C 43.93, 44.07; H 3.02, 3.05; N 5.81, 5.99. C_9H_7NClBr. Calculated %: C 44.20; H 2.88; N 5.73.

α-Chloro-β-(p-bromophenyl)propionic acid (V). Fifteen grams of (XII) was heated with a mixture of 20 ml of 85% formic acid and 8 ml of concentrated hydrochloric acid in a flask under reflux for 5 hours. We obtained 15.9 g of (V). White crystalline compound with m. p. 101-101.5°. Yield 97.5%.

Found %: C 41.34, 41.29; H 6.78, 6.80. $C_9H_8O_2ClBr$. Calculated %: C 41.00; H 6.85.

α-Chloro-β-(p-nitrophenyl)propionic acid (VI). We obtained 5.39 g of (VI) from 5 g of α-chloro-β-(p-nitrophenyl)propionitrile. Yield 98%. Lemon-yellow crystalline powder with m. p. 119-120°. Literature data: m. p. 121-122° [7].

α-Bromo-β-phenylpropionic acid (VII). We obtained 27.2 g of (VII) from 30 g of α-bromo-β-phenylpropionitrile [1]. Yield 85%. White crystals with m. p. 48° (from water). Literature data: m. p. 48° [8].

Ethyl α-chloro-β-phenylpropionate. A solution of 5 g of (XI) in 4 ml of anhydrous ethyl alcohol was saturated at 0° with dry hydrogen chloride; the imino ester hydrochloride of α-chloro-β-phenylpropionic acid was obtained as a precipitate which rapidly hydrolyzed on the filter and was converted into the ethyl ester of the same acid. Colorless oil with a weak ester odor, b. p. 85-89° at 50 mm. Literature data: b. p. 134-135° (at atmospheric pressure) [2].

α-Chloro-β-phenylisobutyric acid (VIII). The methyl ester of acid (VIII) [9] (9.8 g) was heated for 18 hours with a mixture of 20 ml of 85% formic acid and 15 ml of concentrated hydrochloric acid. The reaction mixture after cooling was diluted with an equal volume of water and the separated oil was extracted with ether. The ether layer was separated and dried over sodium sulfate. Removal of the ether by evaporation and vacuum-distillation of the residue gave 4.5 g of (VIII). Yield 49%. The compound is an oil with b. p. 162-165° at 5 mm.

Attempts to obtain the anilide proved unsuccessful. The phenylhydrazide of acid (VIII) has m. p. 93-94°

Found %: N 9.60, 9.52. $C_{16}H_{17}ON_2Cl$. Calculated %: N 9.67.

α-Chloro-β-phenylisobutyric acid (VIII) from methacrylic acid. A solution of phenyldiazonium chloride was prepared from 20 ml of aniline and added to a solution of 17.2 g of (X) in 100 ml of acetone. Nitrogen began to evolve (at 19-21°) after the addition of 5 g of cupric chloride and 4 g of magnesium oxide to the reaction mixture. After the usual treatment we obtained 19.8 g of (VIII). Yield 50%. B. p. 159-165° at 5 mm. The phenylhydrazide has m. p. 93-94°; the melting point was not depressed when this hydrazide was mixed with the phenylhydrazide prepared from (VIII), obtained by the hydrolysis of the ester.

α-Chloro-β-(p-nitrophenyl)isobutyric acid (IX). Twenty grams of the methyl ester of α-chloro-β-(p-nitrophenyl)isobutyric acid was heated with 25 ml of 85% formic acid and 10 ml of concentrated hydrochloric acid for 8 hours. Reprecipitation from 1N NaOH solution gave 18.0 g of (IX). Yield 94.5%. M. p. 141-142° (from alcohol). Literature data: m. p. 140-142° [5].

SUMMARY

1. The synthesis of α-halo-β-arylpropionic and α-halo-β-arylisobutyric acids by the saponification of the corresponding nitriles and methyl esters with a mixture of formic and hydrochloric acids was described.

2. α-Chloro-β-phenylpropionic acid, α-chloro-β-(p-methoxyphenyl)propionic acid, α-chloro-β-(2,4-dichlorophenyl)propionic acid, α-chloro-β-(p-bromophenyl)propionic acid, α-chloro-β-(p-bromophenyl)-propionitrile and α-chloro-β-phenylisobutyric acid were synthesized for the first time.

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PREPARATION AND TRANSFORMATION OF p-DIETHYLBENZENE HYDROPEROXIDE

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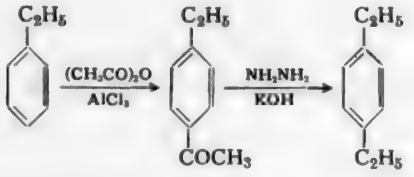
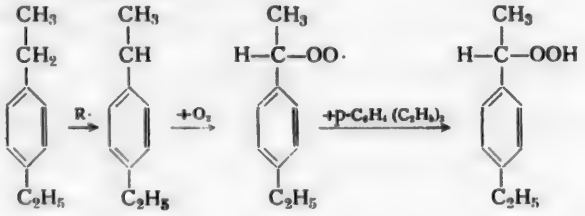
Some years ago a paper appeared by Bergmann and Resnik [1], devoted to a study of the autooxidation of of the individual, highly pure, diethylbenzene isomers. It was shown by the authors that all three diethylbenzene isomers on autooxidation formed a small amount of the corresponding ethylacetophenone isomers (in the oxidation of o-diethylbenzene the amount of o-ethylacetophenone in the reaction mass was found to be equal to 19.3%, and correspondingly, the amounts of m-ethylacetophenone and of p-ethylacetophenone were found to be equal to 42.5% and 30.5%, respectively). A considerable portion of the reaction products went to a tar (up to 30% of tar in the reaction mass) and contained a small amount of the corresponding ethylbenzoic acids (1-5%). The presence of hydroperoxides in the reaction process could not be shown. The reaction was run at 120-130° in the presence of 5% of a mixed chromium oxide-cobalt oxide (4:1) catalyst. It is quite obvious that the drastic conditions under which the mentioned authors ran the reaction made it impossible not only to establish the presence of hydroperoxides, but also to expect any satisfactory yields of the final oxidation products (ethylacetophenones), since under these conditions the extent of oxidation due to the accumulation of by-products, inhibiting the process, could not be great in view of the rupture of the reaction chains.

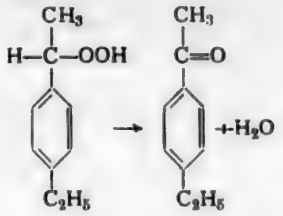
In the present study our problem was to run the autooxidation of p-diethylbenzene under such conditions as would permit the formation of a substantial amount of the hydroperoxide with a greater degree of oxidation.

We selected p-diethylbenzene for the reason that it is the most readily available of the three diethylbenzene isomers. We prepared the p-diethylbenzene by the acetylation of ethylbenzene with acetic anhydride, followed by the reduction of the p-ethylacetophenone using the Kizhner method.

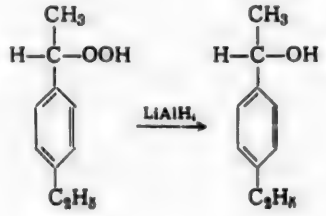


The autooxidation of p-diethylbenzene proceeds with considerable rapidity; the reaction mass after oxidation consists of p-diethylbenzene hydroperoxide, p-ethylacetophenone and unoxidized starting product. The formation of these products proceeds by the schemes

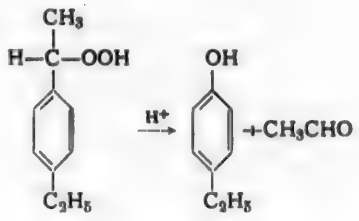




The p-diethylbenzene hydroperoxide was isolated from the reaction mass through the sodium salt. To establish the structure of the concentrated hydroperoxide (92.8%) obtained in this manner we reduced it to methyl-p-ethylphenylcarbinol, which was then dehydrated by heating.



Of interest is the fact that p-diethylbenzene hydroperoxide under the influence of catalytic amounts of concentrated sulfuric acid is decomposed with the evolution of heat and the formation of acetaldehyde and p-ethylphenol, similar to what happens in the acid cleavage of isopropylbenzene hydroperoxide to yield phenol and acetone.



EXPERIMENTAL

The starting p-ethylacetophenone was obtained by the acetylation of ethylbenzene with acetic anhydride in the presence of anhydrous aluminum chloride. The yield was 88%, based on the acetic anhydride. The obtained p-ethylacetophenone had b. p. 85-86° at 3 mm, n_D^{22} 1.5226, d_4^{22} 0.9960. 2,4-Dinitrophenylhydrazone, m. p. 208°. Literature data: b. p. 130° at 23 mm, d_4^{20} 0.991 [2]. 2,4-Dinitrophenylhydrazone, m. p. 208-209° [3].

Preparation of p-diethylbenzene. Into a flask, fitted with a thermometer descending to the bottom, and a Vigreux column, was charged 3 liters of diethylene glycol and then 2 kg of potassium hydroxide was dissolved in the glycol with heating. Then 1000 ml of 80% hydrazine hydrate and 750 g of p-ethylacetophenone was added. The whole mixture was slowly heated, and the reaction products were continuously removed by distillation and condensed in a receiver. The temperature in the flask slowly rose to 260°, after which the reaction was stopped. The distillate was washed with water, then with dilute sulfuric acid, again with water, and dried

over potash. On distillation from metallic sodium the fraction with b. p. 69-71° at 14 mm, and n_D^{20} 1.4945 was collected. The obtained fraction was redistilled through a column having an efficiency of 33 theoretical plates. We obtained 130 g of p-diethylbenzene with b. p. 70° at 14 mm, d_4^{20} 0.860, n_D^{20} 1.4947; literature data [4]: b. p. 183.6° at 760 mm, d_4^{20} 0.8619, n_D^{20} 1.4947.

Autooxidation of p-diethylbenzene. The process was run in a column having a diameter of 3.2 cm and a height of 30 cm, which was filled to one half of its height with glass tube packing (5 × 6 mm), connected to a trap of the Dean–Stark type, a tube for the admittance of air, descending almost to the bottom of the column, and a reflux condenser. The air was passed at a rate of about 2 liters/min through 130 g of p-diethylbenzene at 110°. We added 0.2 g (about 0.15%) of nickel benzoate to initiate the reaction. The reaction mass was sampled at periodic intervals and analyzed for the amount of hydroperoxide (iodometrically) and p-ethylacetophenone (oximation). The course of the autooxidation process is depicted in the Table.

Autooxidation of p-Diethylbenzene

Time (in hours)	3	5	8	11	15	18
Amount of hydroperoxide (in %)	9.08	—	13.16	15.18	16.55	16.4
Amount of ketone (in %)	3.2	—	—	36.5	54.7	58.5
n_D^{22}	1.4990	1.5016	1.5020	1.5040	1.5060	1.5065

The reaction was stopped after 18 hours. The reaction mass weighed 142.5 g. The amount of water evolved during reaction was 9.4 ml.

Isolation of the Hydroperoxide. With cooling to 5° and stirring, 140 g of the reaction mass was slowly added to a solution of 15 g of sodium hydroxide in 200 ml of water. After all of the reaction products had been added the alkaline layer (a) was separated from the oil layer (b). The alkaline layer was extracted with ether. Then a stream of carbon dioxide was passed through it until completely saturated. The liberated oil was separated, the water layer was extracted with ether (twice with 50 ml portions), and the ether extracts were added to the main oil portion. Then the ether was removed by distillation under reduced pressure. The straw yellow residue (29 g) analyzed 92.76% hydroperoxide (determined iodometrically); n_D^{24} 1.5225. About 3 g of the obtained hydroperoxide was purified again through the sodium salt by the above-described method. The concentration of the hydroperoxide rose to 94.2%, n_D^{24} 1.5231. For further reactions we used the hydroperoxide with a peroxide content of 92.76%.

Isolation of p-ethylacetophenone. The reaction mass after oxidation and isolation of the hydroperoxide (oil layer b) was washed with water, then dried over anhydrous sodium sulfate, and finally distilled under reduced pressure. We obtained 12.5 g of unoxidized p-diethylbenzene and 95 g of p-ethylacetophenone with b. p. 85-87° at 3 mm, n_D^{20} 1.5230. The 2,4-dinitrophenylhydrazone melted at 207-208°.

Thermal decomposition of the hydroperoxide. A solution of 3 g of the obtained hydroperoxide in 20 ml of tert-butylbenzene was heated at 130° until all of the hydroperoxide had decomposed (3 hours). The obtained dark-red reaction mass was distilled under reduced pressure. About 2.4 g of p-ethylacetophenone was isolated.

Reduction of the hydroperoxide. To a suspension of 1 g of aluminum lithium hydride in 20 ml of ether, with cooling to −10°, was gradually added with stirring a solution of 7.6 g of the hydroperoxide in 25 ml of dry ether. Then the mixture was stirred for 1 hour at a temperature not exceeding +10°, after which the excess aluminum lithium hydride was decomposed at first with moist ether, then with water, and finally with 25 ml of 10% sulfuric acid. The ether layer was separated, dried over potash, and the ether was distilled off. The residue was distilled under reduced pressure. We obtained 5.4 g of oily substance with b. p. 121-122° at 15 mm. Literature data [5]: boiling point of methyl-p-ethylphenylcarbinol 119.5° at 14 mm. Yield of the carbinol 80%.

Acid decomposition of the hydroperoxide. Five grams of p-diethylbenzene hydroperoxide was dissolved in 15 ml of benzene. To the obtained solution with vigorous stirring and cooling to 10° was added a drop of concentrated sulfuric acid. The presence of hydroperoxide in the reaction mass could not be detected after stirring for 1 hour. The solution was distilled at atmospheric pressure. The 1st fraction consisted of a substance with b. p. 20-23° (several drops). Then practically pure benzene distilled off. The residue (about 3 g) distilled at 205-215° and gradually crystallized in the receiver. After recrystallization from alcohol the obtained substance melted at 46°; literature data [6] for p-ethylphenol: m. p. 47-48°. The substance is completely alkali-soluble, and gives a blue-violet color with aqueous ferric chloride solution.

The 1st fraction with b. p. 20-23° gives a bright color with fuchsin-sulfurous acid solution and is apparently acetaldehyde, not exactly identified.

SUMMARY

1. The autooxidation of p-diethylbenzene gave for the first time the corresponding monohydroperoxide.

2. The structure of the hydroperoxide was shown by its conversion into p-ethylacetophenone, methyl-p-ethylphenylcarbinol and p-ethylphenol.

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SYNTHESIS OF ALKALOID MAGNOLAMINE

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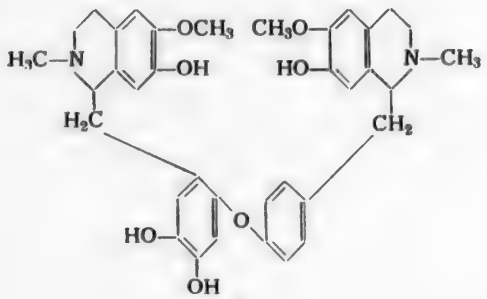
Magnolamine, one of the group of bisbenzyltetrahydroisoquinoline monoethers, was isolated in 1938 by A. P. Orekhov and N. F. Proskurnina [1] from the leaves of Magnolia fuscata. The structure of the alkaloid was established by the oxidation of its ethers. The treatment of the methyl ether of magnolamine with potassium permanganate gave [2] three substances: 1-keto-2-methyl-6,7-dimethoxytetrahydroisoquinoline, identified with the compound isolated earlier from alkaloids of this series; magnolaminic acid; and the corresponding dialdehyde. Magnolaminic acid is a dibasic acid, contains two methoxyl groups, and belongs to the class of diphenyl ether derivatives. The fusion of this acid with alkali led to 4-hydroxybenzoic acid, but a second acid could not be isolated. As a result, it was shown that both of the methoxyl groups are located in one ring of the diphenyl ether. To establish the structure of the alkaloid a number of similar dicarboxylic acids with a variable distribution of the methoxyl groups were synthesized [2-4]. In 1951, 3,4-dimethoxy-4',6-dicarboxydiphenyl ether [4] was obtained, identical with magnolaminic acid. Since this alkaloid contains four free hydroxyl groups, a study was made of the oxidative decomposition of its tetraethyl ether.

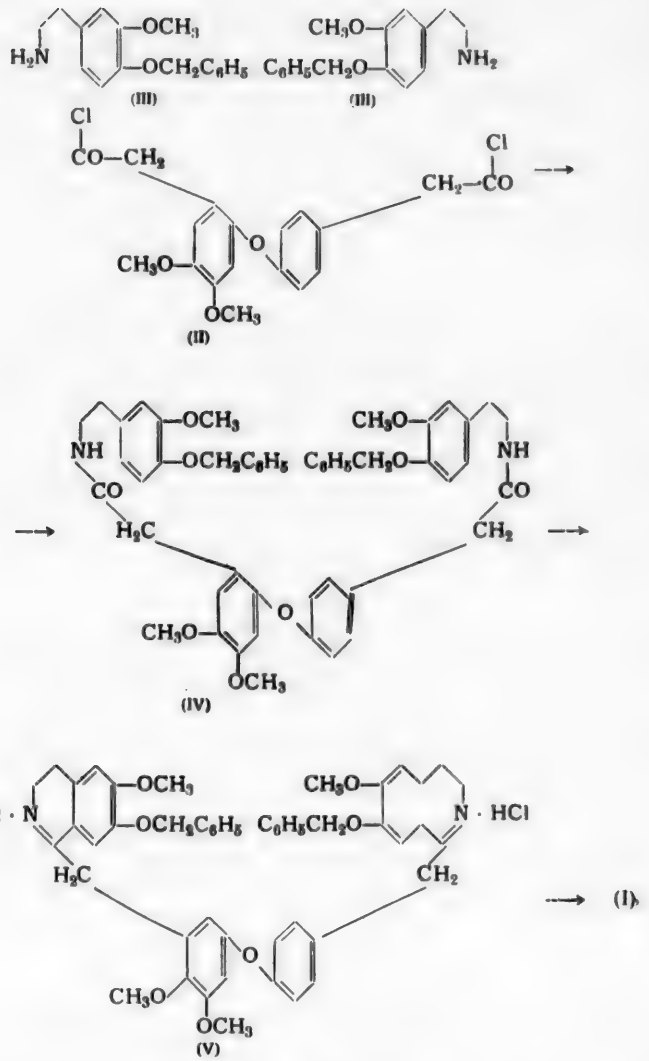
On the basis of the performed studies the following formula (I) was proposed for magnolamine.



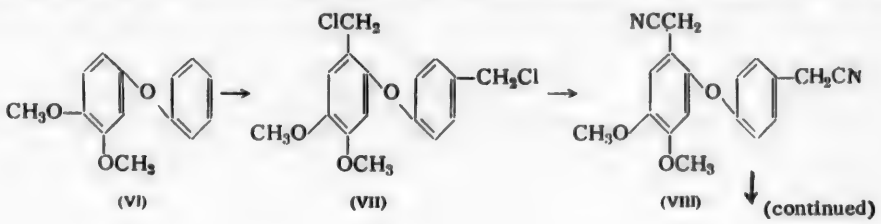
(I)

The final structure of the alkaloid can be confirmed by its complete synthesis.

In the present study we accomplished the preparation of the main intermediate in the synthesis of the dimethyl ether of magnolamine. Condensation of the dichloride of 3,4-dimethoxy-4',6-dicarboxymethyldiphenyl ether (II) with β-(3-methoxy-4-benzyloxy)phenylethylamine (III) gave the diamide (IV). Simultaneous closure of the two isoquinoline rings led to the dihydrochloride of 3',4'-dimethoxy-4',6-[bis(6-methoxy-7-benzyloxy)-3,4-dihydroisoquinolyl]dimethyldiphenyl ether (V). Further hydrogenation, methylation and removal of the benzyl radicals, not representing any special difficulties, should lead to the dimethyl ether of magnolamine.



3,4-Dimethoxy-4',6-dicarboxymethyldiphenyl ether (II) was obtained by two methods. 1) The chloromethylation of 3,4-dimethoxydiphenyl ether (VI) led to compound (VII). Then the chlorine was replaced by the nitrile group, and the corresponding dicyanide (VIII) was saponified to the dicarboxylic acid (IX).



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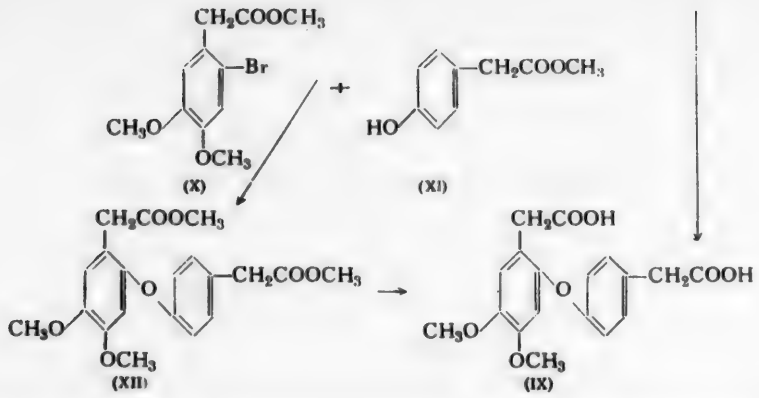

The methyl ester of 2-bromo-3,4-dimethoxyphenylacetic acid (X) was condensed with the methyl ester of 4-hydroxyphenylacetic acid (XI) by the Ullmann reaction. In both cases the yields were small; however the first method, since it includes a smaller number of steps (taking into consideration the synthesis of the starting materials), is to be preferred to the second method. The most difficult is the chloromethylation reaction, which was run in the presence of either formalin or trioxymethylene under various temperature conditions. In all cases the yields, determined by the amount of final product, were small—of the order of 3%; the formation of the chloromethyl derivative was not observed at a temperature of 0°. The position of the chloromethyl groups was confirmed by the oxidation of compound (VII) and the isolation of magnolaminic acid, and also by the identity of the dicarboxylic acids obtained by the two methods.

EXPERIMENTAL

3,4-Dimethoxy-4',6-dichloromethyldiphenyl ether (VII). To a solution of 5 g of 3,4-dimethoxydiphenyl ether [5] (VI) in 20 ml of glacial acetic acid was added 3.6 g of 38.4% of formalin, and then with vigorous stirring a rapid stream of dry hydrogen chloride was passed into the mixture for 2 hours at 30°. Then the reaction mass was poured over ice, the separated oil was extracted with benzene, washed with soda solution, then with water, and dried over calcium chloride. The viscous oil (5.9 g) that remained after removal of the solvent was used without further purification for the next synthesis.

Oxidation of the obtained substance with potassium permanganate in boiling aqueous acetone solution gave a brown-colored compound. Two recrystallizations from acetone gave the substance as colorless crystals with m. p. 283-284°. This corresponds to the melting point of 3,4-dimethoxy-4',6-dicarboxydiphenyl ether [4].

Found %: C 60.48; H 4.53. $C_{16}H_{14}O_7$. Calculated %: C 60.38; H 4.43.

3,4-Dimethoxy-4',6-dicyanomethyldiphenyl ether (VIII). A solution of 5.9 g of (VII) in 20 ml of acetone was gradually added to a hot solution of 12 g of potassium cyanide in 30 ml of ethyl alcohol and 15 ml of water. The reaction mixture was heated at the boil for 4 hours. The solvent was distilled off, the obtained substance was extracted with benzene, and the extract was washed with water and dried over calcium chloride. Removal of the benzene left a brownish viscous oil which was used for the next synthesis.

Preparation of 3,4-dimethoxy-4',6-dicarboxymethyldiphenyl ether (IX). a) To a solution of 4.3 g of the impure dicyano derivative (VIII) in 26 ml of ethyl alcohol was added 16 ml of 50% aqueous potassium hydroxide solution and the whole heated at the boil for 15 hours. After removal of the alcohol in vacuo the nonacidic impurities were extracted with chloroform. The water layer, with cooling, was slowly treated with dilute hydrochloric acid until acid. A yellowish oil separated that gradually solidified. Three recrystallizations from water (with the addition of animal charcoal) gave colorless crystals. Yield 0.25 g (3.33%), based on the 3,4-dimethoxydiphenyl ether. M. p. 141.5-143°.

Found %: C 62.76, 62.57; H 5.02, 5.19. $C_{18}H_{18}O_7$. Calculated %: C 62.42; H 5.24.

b) To a solution of 2.9 g of potassium metal in 15 ml of anhydrous ethyl alcohol was added a solution of 8.63 g of methyl 4-hydroxyphenylacetate in 20 ml of benzene. The alcohol and benzene were distilled off in vacuo. The residue was dried by adding benzene and then distilling it off, and finally by heating in a vacuum of 2 mm at a temperature of 70-80°. Then 19.6 g of methyl 3,4-dimethoxy-6-bromophenylacetate,* 1.8 g of copper catalyst and 1.5 g of anhydrous copper sulfate were added. The reaction mixture was heated in a stream of nitrogen for 4 hours at 180-190°. The semisolid reaction mass after cooling was extracted with ether, the extract washed with 2% sodium hydroxide solution, then with water, and dried over sodium sulfate. After removal of the ether the methyl ester of 3,4-dimethoxy-6-bromophenylacetic acid was distilled off at a vacuum of 1 mm and a temperature of 135-140°. The residue was dissolved in 15 ml of methyl alcohol, a solution of 0.1 g of sodium hydroxide in 30 ml of water was added, and the whole was allowed to stand for 2.5 hours. The alcohol was vacuum-distilled, while the water layer was extracted with ether and then acidified with dilute hydrochloric acid (to Congo). Repeated recrystallization from water (with the addition of animal charcoal) gave colorless crystals with m. p. 141.5-143°. Yield 0.9 g (5%). The compound does not depress the melting point when mixed with the 3,4-dimethoxy-4',6-dicarboxymethyldiphenyl ether obtained by method "a."

Bis[β-(3-methoxy-4-benzyloxy)phenylethylamide] of 3',4'-dimethoxy-4',6-dicarboxymethyldiphenyl ether (IV). A mixture of 0.93 g of 3,4-dimethoxy-4',6-dicarboxymethyldiphenyl ether and 1.94 ml (3.37 g) of thionyl chloride was heated at 50-60° for 2 hours. The excess thionyl chloride was removed by vacuum-distillation. The residue was dissolved in 20 ml of chloroform and then added gradually to a chloroform solution of 2.08 g of β-(3-methoxy-4-benzyloxyphenyl)ethylamine. Approximately 7.8 ml of 5% potassium hydroxide solution was added simultaneously with this, constantly maintaining a weakly alkaline medium (to phenolphthalein). Then the reaction mass was stirred for 30 minutes, the chloroform layer separated, washed with 5% hydrochloric acid, then with water until neutral, and finally dried over sodium sulfate. The residue after removal of the solvent was viscous brownish oil, which when rubbed in anhydrous ether gave a slightly yellow powder with m. p. 106-109°. Yield 2 g (90%). Two recrystallizations from ethyl alcohol (with the addition of animal charcoal) gave the compound as colorless crystals. M. p. 127-130°.

Found %: C 73.16, 73.14; H 6.24, 6.39; N 3.48, 3.54. $C_{50}H_{52}O_9N_2$. C 72.80; H 6.25; N 3.40.

3',4'-Dimethoxy-4',6-[bis(6-methoxy-7-benzyloxy)-3,4-dihydroisoquinolyl]dimethyldiphenyl ether dihydrochloride (V). To a solution of 0.3 g of ether (IV) in 2 ml of chloroform was added with cooling a solution of 0.3 g of phosphorus pentachloride in 10 ml of chloroform. The reaction mixture was allowed to stand for 3 days at room temperature and then was heated at the boil for 1 hour. After cooling well the mixture was washed with water, then with 2% sodium hydroxide solution, treated with dilute hydrochloric acid, then with water until neutral, and finally dried over sodium sulfate. The residue after removal of the chloroform in vacuo was rubbed in dry ether to give a yellowish powder. The latter was precipitated twice from anhydrous alcohol with ether, and dried in vacuo at 1-2 mm and 60° for 3-4 hours. Yield 0.26 g (83.2%). M. p. 137-140° (decompn.).

Found %: C 69.28, 69.38; H 6.03, 5.70; N 3.30. $C_{50}H_{48}O_7N_2 \cdot 2HCl$. Calculated %: C 69.68; H 5.85; N 3.25.

SUMMARY

We accomplished the preparation of 3',4'-dimethoxy-4',6-[bis-(6-methoxy-7-benzyloxy)-3,4-dihydroisoquinolyl]dimethyldiphenyl ether dihydrochloride—the principal intermediate in the synthesis of the dimethyl ether of the alkaloid magnolamine.

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* Colorless crystals with m. p. 65-66°. B. p. 133-135° at 1 mm. Obtained from 3,4-dimethoxy-6-bromophenylacetic acid [6].

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ALKALOIDS OF FOUR SPECIES OF UNGERNIA

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Alkaloids of the plants of genus Ungernia (family Amaryllidaceae) have received little chemical and pharmacological study. Of the 6 species of ungernia [1], found growing in the mountain regions of Central Asia, the alkaloids of two of the species have been studied earlier. In particular, A. P. Orekhov and S. S. Norkina isolated tazettine [2] from Ungernia Severtzovii (Rgl.) B. Fedsch., while N. K. Yurashevsky isolated lycorine [3] from the bulbs of Ungernia tadschicorum Vved.

In studying the alkaloids of U. Severtzovii, collected near the village of Brich-Mulla (Tashkent region)* in May of 1949, in the preflowering stage, we established that the bulbs contain 0.7%, the skins of the bulbs 0.11%, and the above-ground portion of the plant 0.29% of total alkaloids.

On separating the mixed alkaloids found in the bulbs we obtained three crystalline bases [4]. The first of them gives a number of crystalline salts. The free alkaloid was isolated by decomposing the purified hydrochloride.

On the basis of elemental analysis of the base itself, and also of the nitrate, we established this alkaloid to have the composition $C_{19}H_{23}NO_5$ and gave it the name of ungerine.

Of the five oxygen atoms in ungerine one is found present as a methoxyl group, and another two are present as a methylenedioxy group. The presence of aldehyde, ketone and hydroxyl groups could not be shown. The nitrogen in this alkaloid is tertiary and does not have an N-methyl group. The catalytic hydrogenation of ungerine gave dihydroungerine $C_{19}H_{25}NO_5$. As a result, ungerine has the following, partially developed formula:

$$C_{17}H_{18}O_2(>N-)\,(CH_2O_2)\,(OCH_3)\,(=)$$

After removal of the ungerine, we isolated tazettine from the remaining mixture of alkaloids, making use of their different solubility in acetone and alcohol.

The third alkaloid, isolated from the bulbs of U. Severtzovii, proved to be new, and we named it ungeridine. It has the composition $C_{20}H_{25}NO_4$, contains one methylenedioxy group, one methoxyl, and a nonphenolic hydroxyl group. When heated with acetic anhydride it gives a monacetyl derivative. The nitrogen of ungeridine is tertiary and does not have an N-methyl group. The base is unsaturated; its hydrogenation gave dihydroungeridine. Consequently, ungeridine has the following developed formula:

$$C_{18}H_{19}(>N-)\,(CH_2O_2)\,(OCH_3)\,(OH)\,(=)$$

On separating the mixture of alkaloids found in the above-ground portion of U. Severtzovii it was established that the same three alkaloids are also present here: ungerine, ungeridine and tazettine [5]. We did not make a detailed chemical study of the skins of the bulbs of U. Severtzovii.

* All of the species of ungernia investigated by us were collected by E. E. Korotkov.

From the bulbs of U. Severtzovii, collected in April of 1956 in Karshan-Tau of the Kazak SSR, in the preflowering stage, we isolated 2% of total alkaloids, from the skins of the bulbs – 0.23%, from the rootlets with the butt ends of the bulbs – 2.28%, and from the above-ground portion – 0.75%. The main constituents in the total alkaloids proved to be lycorine and ungerine.

From the bulbs of Ungernia tadshicorum Vved., collected in July of 1952 on the Hissar ridge, in the withering stage of the above-ground portion, we isolated 0.3% of total alkaloids. Lycorine and ungeridine [6] were isolated from the mixture of alkaloid bases.

Ungernia Victoris Vved. was collected in July of 1956, in the withering stage of the above-ground portion, from the Surkhan-Daryinsk region of Uzbekistan. It was established that the bulbs of U. Victoris contain 0.45%, the skins of the bulbs – 0.11%, and the rootlets with butt end – 2.5% of mixed alkaloids. The total alkaloids, isolated from the bulbs and roots, were found to contain 30% of galanthamine [6], isolated earlier from the bulbs of Galanthus Woronowii [7], and 16.2% of lycorine.

Ungernia ferganica Vved. was collected in July of 1955 in the Dzhalal-Abadsk region, in the withering stage of the above-ground portion. The bulbs of this plant contain 0.85%, the skins of the bulbs – 0.15%, and the rootlets with butt end – 1.7% total alkaloids. Tazettine and lycorine were isolated from this mixture of alkaloids.

The pharmacological testing of the alkaloids galanthamine, ungerine, ungeridine and lycorine was done by M. D. Mashkovsky [8].

EXPERIMENTAL

Alkaloids from Ungernia Severtzovii (Rgl.) B. Fedsch.

Twenty three kilograms of air-dried, finely ground, skin-free bulbs of U. Severtzovii was moistened with 10% ammonia solution and then percolated with dichloroethane. The dichloroethane extract was treated with 10% sulfuric acid. The acid solution was washed with ether and then saturated with ammonia gas, after which the alkaloids were extracted with chloroform. Removal of the solvent by distillation left a residue of 162 g of noncrystalline total alkaloids, which represents 0.7% of the weight of dry bulbs.

Ungerine. The mixture of alkaloids (162 g) was dissolved in ethyl alcohol. Then an alcoholic solution of hydrochloric acid was added with cooling. Here the crystalline ungerine hydrochloride (46.3 g) with m. p. 265-266° began to deposit immediately. Two recrystallizations from 70% alcohol raised the melting point to 270-271° (with decompn.). Yield 41 g $[\alpha]_D^{20}$ + 130.73° (c 1.178; water).

The addition of 25% ammonia solution to a water solution of ungerine hydrochloride immediately gave a white crystalline precipitate of ungerine. After two recrystallizations from 70% alcohol the compound melted at 135-136°. Ungerine is readily soluble in acetone, chloroform, ether and alcohol. It is difficultly soluble in petroleum ether and benzene, and insoluble in water. $[\alpha]_D^{20}$ + 116.95° (c 1.274; chloroform).

Found %: C 66.09; H 6.65; N 4.24; OCH_3 10.07; equ. 345.56. $C_{19}H_{23}NO_5$. Calculated %: C 66.06; H 6.71; N 4.05; OCH_3 8.98; equ. 345.36.

Ungerine hydrobromide (obtained in acetone), m. p. 287-288° (with decompn.). $[\alpha]_D^{22}$ + 102.53° (c 1.502 water).

Ungerine nitrate (obtained in alcohol). M. p. 260° (with effervescence).

Found %: C 55.20; H 5.33; N 6.78. $C_{19}H_{23}NO_5 \cdot HNO_3$. Calculated %: C 55.87; H 4.68; N 6.85.

Ungerine methiodide. When methyl iodide was added to an acetone solution of ungerine the crystalline methiodide with m. p. 253-254° precipitated immediately. After 2 recrystallizations from 80° alcohol it melts at 265-266°. $[\alpha]_D^{22.5}$ + 103.83° (c 1.034; water).

Found %: I 26.14. $C_{19}H_{23}NO_5 \cdot CH_3I$. Calculated %: I 26.05.

Dihydroungerine. A solution of 0.72 g of ungerine in 20 ml of 10% acetic acid was shaken with hydrogen in the presence of platinum, prepared by the Adams method from 1.0 g of ammonium chloroplatinate. The

amount of hydrogen absorbed was 55 ml (theory for one double bond is 46 ml). The liquid was suction-filtered from the catalyst, the catalyst washed with water, the acid solution made alkaline, and the base extracted with ether. Evaporation of the ether solution gave needle crystals with m. p. 138-139°. $[\alpha]_D^{21} -29.26°$ (c 1.230; methanol).

Found %: N 4.11. $C_{19}H_{25}NO_5$. Calculated %: N 4.03.

Tazettine. The alcoholic mother liquor containing hydrochloric acid, remaining after removal of the ungerine from the mixed alkaloids, was poured into a dish, where a dark-red tarry residue remained after volatilization of the alcohol. The residue was dissolved in water and made alkaline with ammonia solution; then the alkaloids were exhaustively extracted with ether. Removal of the solvent by distillation gave a light yellow oily residue (118 g). The latter was stirred with 50 ml of acetone, and here a portion of the base crystallized. The crystals were suction filtered and washed with acetone. Yield 8.9 g; m. p. 210-211°; $[\alpha]_D^{32.5}$ 148.17° (c 1.397; chloroform). This alkaloid proved to be tazettine.

Ungeridine. The acetone-containing mother liquor, remaining after removal of the tazettine, was evaporated to remove solvent. The obtained light yellow oily residue (101.2 g) was treated with 50 ml of alcohol. Here a portion of the total alkaloids crystallized (57 g). The crystals had m. p. 195-196°. After 2 recrystallizations from alcohol, m. p. 200-201°. Ungeridine is soluble in acetone, methanol, chloroform and ether, and difficultly soluble in alcohol, benzene and petroleum ether. $[\alpha]_D^{23}$ +153° (c 1.098; chloroform).

Found %: C 69.69; H 6.91; N 4.52; OCH_3 9.45; OH 6.64; equ. 347.35. $C_{20}H_{25}NO_4$. Calculated %: C 70.19; H 7.06; N 4.02; OCH_3 9.07; OH 4.97; equ. 342.18.

Ungeridine picrate, m. p. 190-191°.

Ungeridine methiodide, m. p. 179-180°.

Found %: I 27.46. $C_{20}H_{25}NO_4 \cdot CH_3I$. Calculated %: I 26.16.

Dihydroungeridine. A solution of 0.51 g of the base with m. p. 200-201° in 60% acetic acid was hydrogenated in the presence of 0.3 g of platinum black. The amount of hydrogen absorbed was 45 ml, which corresponds to the saturation of one double bond. The liquid was suction-filtered from the catalyst, the catalyst was washed with dilute acetic acid solution, and the acetic acid solution was extracted twice with ether. Then the acid aqueous solution was made alkaline with ammonia and again extracted with ether. Evaporation of this ether extract resulted in the deposition of the crystalline dihydroungeridine with m. p. 164-165°. Some of the dihydroungeridine was converted to the crystalline hydrochloride with m. p. 168-169°, and to the picrate with m. p. 203-204°.

Alkaloids from ungernia tadshicorum vved. The crystalline mixture of alkaloids (30.5 g) was washed with hot acetone 3 times; after this the crystals had m. p. 239-241°. The base purified in this manner was treated with 5% hydrochloric acid solution. Complete solution occurred at first, and then after some time the hydrochloride (19 g) deposited as needle crystals with m. p. 210-211°. Decomposition of the hydrochloride gave lycorine with m. p. 265-266°. The acetone-containing mother liquor, remaining after removal of the lycorine, was distilled to remove the acetone. Here a brownish residue was obtained, which crystallized when rubbed with a small volume of alcohol. The crystals were separated, and washed with alcohol. Yield 2 g. M. p. 200-201°. The mixed melting point with authentic ungeridine was not depressed.

Alkaloids from ungernia victoris vved. The isolation of the alkaloids from 50 kg of bulbs was effected by extraction with dichloroethane. Treatment of the acid solution with ammonia gas until alkaline resulted in the precipitation of technical lycorine (22.5 g). The alkaloids in the aqueous mother liquor were extracted with chloroform. Removal of the solvent by distillation gave 177 g of total alkaloids. Treatment of the total alkaloids with acetone gave another 10 g of lycorine. The addition of hydrobromic acid to the acetone mother liquor gave a precipitate of galanthamine hydrobromide (78 g). M. p. 255-256° (with decompn.). $[\alpha]_D^{18} -89.91°$ (c 1.379; water).

Found %: Br 21.79. $C_{17}H_{21}NO_3 \cdot HBr$. Calculated %: Br 21.69.

Decomposition of the hydrobromide gave galanthamine with m. p. 127-128°. $[\alpha]_D^{18}$ −117.21° (c 1.220; alcohol).

Alkaloids from ungernia ferganica vved. The extraction of 500 g of bulbs with chloroform gave 4.28 g of total alkaloids (0.85% on the weight of dry bulbs). The obtained mixture of alkaloids was boiled with alcohol; here 0.07 g of lycorine with m. p. 256-257° remained undissolved. Treatment of the alcohol-soluble portion of the mixed bases with acetone gave 2 g of tazettine.

SUMMARY

Tazettine, lycorine and two new alkaloids were isolated from the bulbs of Ungernia Severtzovii. The two new alkaloids are ungerine $C_{19}H_{23}NO_5$ or $C_{17}H_{15}O_2(>N-)(CH_2O_2)(OCH_3)$ (=): and ungeridine $C_{20}H_{25}NO_4$ or $C_{18}H_{19}(>N-)(CH_2O_2)(OCH_3)(OH)$ (=).

Lycorine and ungeridine were isolated from the bulbs of Ungernia tadshicorum.

Galanthamine and lycorine were isolated from the bulbs of Ungernia Victoris.

Tazettine and lycorine were isolated from the bulbs of Ungernia ferganica.

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ALKALOIDS OF PEGANUM HARMALA L.

I. ISOLATION OF TWO NEW ALKALOIDS

N. I. Koretskaya

The alkaloids found in the African rue (Peganum harmala L.) have long attracted the attention of investigators. Harmaline [1], harmine [2], harmalol [3] and dl-peganine (vasicine) [4, 5] have been isolated from the seeds of this plant, while l-peganine [6] has been obtained from the flowering runners.

The dried above-ground portions of Peganum harmala L., gathered in the flowering phase in the foothills of Kirghiz Alatau by an expedition from the All-Union Chem. Pharm. Research Inst. under the direction of P. S. Massagetov, served as the raw material for our investigation. Extraction of the plant material with isopropyl alcohol gave 1.87% of total alkaloids, the main portion of which (1.33% on the weight of raw material) was an alkaloid identical with dl-peganine, as can be seen from the data presented in the Table.

Melting Points of Alkaloids

	Alkaloid from Peganum harmala L. $C_{11}H_{12}ON_2$	Peganine [7] $C_{11}H_{12}ON_2$
Free base	198-199° (with decompn.) or 211-212° (in vacuum)	198° (with decompn.) or 211-212 (in vacuum)
Hydrochloride	203.5-204.5	208
Methiodide	186.5-187.5	187

Chromatographing the tarry residue after separation of the peganine on Al_2O_3 enabled us to isolate harmine (0.0025%) and two new substances—alkaloid No. 1 with composition $C_{11}H_{10}ON_2$ (0.094%) and alkaloid No. 2 with composition $C_{11}H_{10}O_2N_2$ (0.054%).

To make a comparative study of peganine and the newly isolated alkaloids we had their infrared absorption spectra taken.* The infrared absorption spectrum of peganine shows bands at 3110 cm^{-1} (—OH) and 1628 cm^{-1} (—N=C), which is in agreement with its structure. The band, characteristic for the OH group, is absent in the spectrum of alkaloid No. 1, while the band at 1616 cm^{-1} (—N=C) is retained and a band appears at 1675 cm^{-1} (α,β-conjugated or amide carbonyl). The infrared absorption spectrum of alkaloid No. 2 shows bands at 3110 cm^{-1} (—NH or —OH) and 1668 cm^{-1} (α,β-conjugated or amide carbonyl).

An investigation of the structure of both alkaloids is being continued.

EXPERIMENTAL

* Taken in the Physical Chemical Laboratory of the All-Union Chem. Pharm. Research Inst. by a group under the direction of Yu. N. Sheinker.

EXPERIMENTAL

1. Isolation of alkaloids. We used 80% isopropyl alcohol to exhaustively extract 24.3 kg of dry, pulverized, upper plant parts. The extract was evaporated to a volume of 15 liters and then acidified with 4 liters of 25% acetic acid. The chlorophyll and other nonbasic substances were removed by repeated shaking with ether; the acid extract was made alkaline with 25% ammonia and then extracted with chloroform. The semicrystalline mass, remaining after evaporation of the chloroform extract, was rubbed with acetone. The crystalline substance (323 g, part A) was filtered and washed with acetone. The acetone filtrate was evaporated in vacuo, the residue was dissolved in chloroform, and the alkaloids were extracted with 5% acetic acid. The acetic acid extract was made alkaline and then extracted with chloroform to give 114 g (part B) of a tarry mixture of bases. The chloroform solution after extraction with acetic acid was washed with 5% ammonia, then with water, dried, and evaporated to dryness. The residue was 9.0 g of tarry mass (part C).

Both the mixture of total alkaloids and its component parts were subjected to chromatographing on Leningrad Factory No. 2 rapid-filtering paper. The solvents used by us were butyl alcohol, saturated with 5% acetic acid (system I), and isoamyl alcohol, saturated with 5% acetic acid (system II), while to develop the chromatograms we used either Dragendorff reagent or a water solution containing 1% $KMnO_4$ and 1% Na_2CO_3.

2. Identification of the crystalline substance (Part A). The paper chromatographing of part A revealed the presence of one alkaloid with R_f 0.48 (system I) and 0.23 (system II). After repeated recrystallization from methanol and distillation at 170-180° (0.1 mm) the base has m. p. 198-199° (with decompn.) or 211-212° (when melted in vacuum); $[\alpha]_D^{20}$ 0° (c 1.0; $CHCl_3$); hydrochloride, m. p. 203.5-204.5°; methiodide, m. p. 186.5-187.5°. These constants agree with the corresponding constants for dl-peganine.

3. Separation of noncrystalline mixed bases. a) Part B. The paper chromatogram of part B in system I revealed the presence of stains with R_f 0.05, 0.33, 0.48, 0.66, and 0.85 (developer: Dragendorff reagent), and 0.75 (developer; a water solution of 1% $KMnO_4$ and 1% Na_2CO_3). A solution of 114 g of mixed bases in 800 ml of dry chloroform was chromatographed on 2000 g of Al_2O_3. For the leaching we used chloroform (fractions 1-18) and methanol-containing chloroform: 1% CH_3OH (fractions 19-27), 5% CH_3OH (fractions 28-41), 10% CH_3OH (fractions 42-48), and 50% CH_3OH (fractions 49-63). We collected 1 liter of eluate for each fraction.

From fractions 1-18 we isolated 19.28 g of crystalline alkaloid No. 1; from fractions 19-25 and 49 we isolated 0.6 g of a base with m. p. 255-256°, and R_f 0.34 (system I). A depression of the melting point was not observed when this substance was mixed with harmine (R_f 0.34 in system I). From fractions 26-41 we isolated 12.48 g of crystalline alkaloid No. 2, and from fractions 42-48 we isolated 0.3 g of peganine.

b) Part C. The chromatographing of a solution of 9 g of mixed bases in 75 ml of chloroform on 150 g of Al_2O_3 enabled us to isolate 3.54 g of alkaloid No. 1 and 0.75 g of alkaloid No. 2.

4. Alkaloid No. 1. The free base after recrystallization from ether or petroleum ether has m. p. 109.5-110.5°; the substance is readily soluble in benzene, chloroform, ethyl acetate, alcohol, and water; $[\alpha]_D^{20}$ 0° (c 10.0; alcohol); R_f 0.86 (system I, developer-Dragendorff reagent) and 0.83 (system II, and the same developer).

Found %: C 71.11; H 5.38; N 14.71. M 176 (Rast). $C_{11}H_{10}ON_2$. Calculated %: C 70.95; H 5.41; N 15.05. M 186.2.

The hydrochloride was obtained in alcohol solution, m. p. 250-251° (from methanol).

Found %: C 59.73; H 5.29; N 12.53; Cl 16.22. $C_{11}H_{10}ON_2 \cdot HCl$. Calculated %: C 59.33; H 4.98; N 12.59; Cl 15.92.

The hydrobromide was obtained by treating the free base with 48% HBr; m. p. 293° (from alcohol), and distills at 250° (0.1 mm). Picrate, m. p. 188-188.5° (from alcohol).

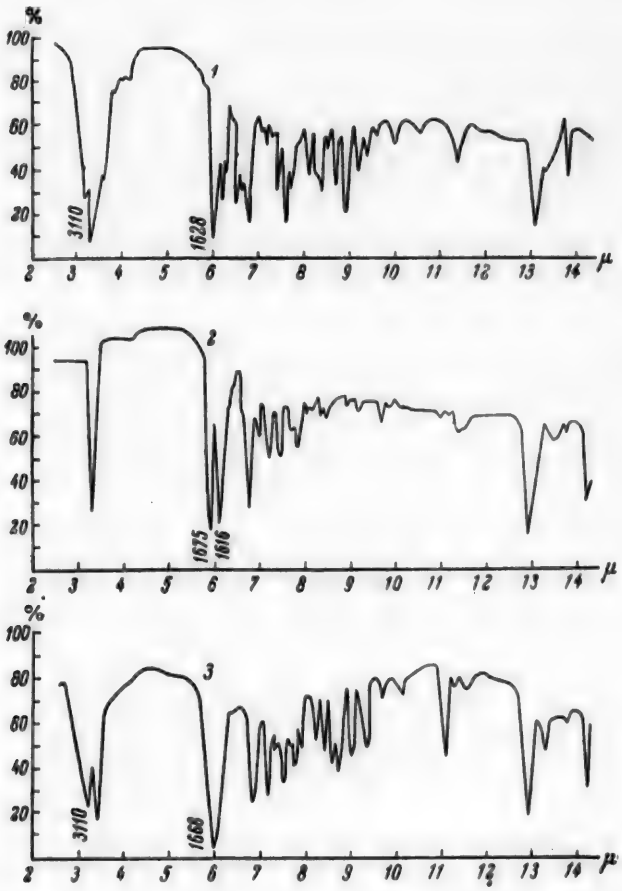
5. Alkaloid No. 2. The free base after recrystallization from water and methanol, and distillation at 140-150° (0.1 mm), has m. p. 203-204°; $[\alpha]_D^{20}$ −129.0° (c 0.7; $CHCl_3$); R_f 0.75 (system I, developer—a water solution of 1% $KMnO_4$ and 1% Na_2CO_3) and 0.70 (system II, and the same developer).

Found %: C 65.28; H 4.95; N 13.68; NCH_3- and OCH_3 absent. M 247 (Rast). $C_{11}H_{10}O_2N_2$. Calculated %: C 65.33; H 4.98; N 13.85 M 202.2.

The hydrochloride was obtained in alcohol solution, m. p. 231-232.5° (from anhydrous alcohol); the hydrochloride is hydrolyzed by water with the separation of the crystalline free base.

Found %: C 55.38; H 4.92; N 11.75; Cl 14.61. $C_{11}H_{10}O_2N_2 \cdot HCl$. Calculated %: C 55.35; H 4.64; N 11.74; Cl 14.86.

Hydrobromide, m. p. 249-250° (from anhydrous alcohol); the hydrobromide is hydrolyzed by water.



Infrared absorption spectra (in vaseline oil). 1) Peganine, 2) alkaloid No. 1, 3) alkaloid No. 2.

SUMMARY

Peganine, harmine and two new substances—alkaloid No. 1 and alkaloid No. 2—were isolated from the above-ground portions of Peganum harmala L.

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ALKALOIDS OF LEUCOJUM AESTIVUM

ISOLATION OF ISOTAZETTINE

N. F. Proskurnina

In the present communication we present the data obtained in studying a number of specimens of the bulbs and leaves of Leucojum aestivum,* gathered in various periods of the growing season from March 15 to April 13, 1956 in the Kobuletsk region of Adzhar Armenian SSR, near the village of Bobokvati. The material investigated by us was gathered by the regional station of Vilar** under the direction of M. M. Molodozhnikov. Lycorine (from 0.05 to 0.13%) and galanthamine (from 0.05 to 0.22%) were isolated from all of the specimens of Leucojum aestivum investigated. Here the amount of lycorine in both the bulbs (0.05-0.06%) and leaves (0.13-0.11%) remains constant, independent of the time of gathering, whereas the amount of galanthamine drops considerably as the plant grows.

In addition to lycorine and galanthamine, we also isolated a third amorphous base with composition $C_{16}H_{21}O_5N$ from the mother liquors, which we were able to purify through its difficultly soluble salts (hydrochloride and hydrobromide). Taking into consideration the fact that the new base has the same composition as tazettine, we have proposed to name it "isotazettine."

The results of investigating the different specimens of Leucojum aestivum are given in Table 1.

TABLE 1

Time of gathering	Plant raw material	Amount of alkaloids in percent on the air-dried material		
		lycorine	galantha-mine	isotazettine
15 March	Bulbs	0.06	0.09	
15 March	Leaves	0.13	0.22	0.03
20 March	Bulbs	0.05	0.13	
20 March	Leaves	0.12	0.11	
13 April	Bulbs	0.06	0.05	0.015
15 April	Leaves	0.11	0.10	

Isotazettine remains amorphous even after careful purification through its salts; however when isotazettine is treated with water, in which it is quite readily soluble, it gradually changes into a crystalline base with the same composition ($C_{16}H_{21}O_5N$), but differing in its properties from the amorphous base. The nearly complete transition (in the cold) of the amorphous isotazettine into the crystalline base requires 10-12 days. The mother liquor from the separation of the crystalline base contains a small amount of unchanged isotazettine.

* From the bulbs of Leucojum vernum L., gathered in June and stored until December, Boit [1] isolated lycorine and homolycorine, whereas the same bulbs stored up to the time of their sprouting (January) contained, in addition to the mentioned alkaloids, galanthamine as the principal alkaloid.

** Vilar—All-Union Institute of Medicinal and Aromatic Plants.

TABLE 2

	Empirical formula	Free base			Hydrochloride		Hydrobromide	
		$[\alpha]_D$	melting point	R_f^*	$[\alpha]_D$	melting point	$[\alpha]_D$	melting point
Tazettine	$C_{18}H_{21}O_5N$	+ 150.4° [2]	210—211° (amorphous)	0.49	+ 115°	201—202°	+ 118.5°	203—204°
Isotazettine	$C_{18}H_{21}O_5N$	+ 66.4	208—210	0.26	+ 24.5	224—225	+ 20.9	230—233
Crystalline base obtained from isotazettine	$C_{18}H_{21}O_5N$	+ 151		0.49	+ 113.7	201—202	+ 119	203—204

The salts of the two bases also show considerable difference in their solubility, melting point and specific rotation.

A comparison of the properties of the crystalline base obtained from isotazettine by treatment of the latter with water, with the properties of tazettine (Table 2), and also the mixed melting point of the crystalline base with tazettine, revealed that these two substances are identical. As a result, isotazettine is apparently an epimer of tazettine.

It could also be assumed that isotazettine is identical with haemanthine, isolated from Boophane disticha [3]. However, due to the absence of data for haemanthine characterizing this alkaloid (only the composition of haemanthine is known, and the fact that it is amorphous), the question as to the identity of these two alkaloids still remains unsolved.

EXPERIMENTAL

The isolation of lycorine and galanthamine from all of the investigated specimens of Leucojum aestivum was done in essentially the same manner as described for the isolation of the alkaloids of Galanthus woronowi [4]. Lycorine was isolated as the free base, while galanthamine was isolated as the difficultly soluble hydrobromide.

Isolation of isotazettine hydrochloride. The mother liquor from the separation of galanthamine hydrobromide was evaporated in vacuo, the residue dissolved in water, made alkaline with ammonia, and extracted with ether. The oily base after removal of the ether was converted to the hydrochloride, which after washing with acetone and 3 recrystallizations from alcohol had m. p. 224-225° and $[\alpha]_D$ + 24.9° (c 0.2; water).

Found %: C 58.87; H 6.13; N 3.94; Cl 9.47. $C_{18}H_{21}O_5N \cdot HCl$. Calculated %: C 58.77; H 5.99; N 3.81; Cl 9.66.

Isotazettine. The base, isolated from the purified hydrochloride, after drying in vacuo (room temperature) was obtained as a slightly yellow glassy mass with $[\alpha]_D$ + 66.4° (c 0.2; chloroform). Isotazettine is readily soluble in organic solvents and in water.

Found %: C 65.02; H 6.28; N 4.01. $C_{18}H_{21}O_5N$. Calculated %: C 65.22; H 6.39; N 4.23.

Isotazettine hydrobromide was recrystallized from a mixture of alcohol and water. M. p. 230-233°, $[\alpha]_D$ + 20.9° (c 0.2; water). Is is very difficultly soluble in alcohol and quite difficultly soluble in water.

Reaction of isotazettine with water. A solution of 0.5 g of isotazettine in 5 ml of water, on being allowed to stand in the cold, began to deposit a crystalline precipitate, the amount of which increased with time: at the end of the first day the amount of crystalline precipitate isolated was 0.19 g, at the

end of the second day another 0.06 g, etc. After 10 days we obtained 0.37 g of crystalline tazettine as the free base with m. p. 200-202°. After washing with water and recrystallization from acetone the free base had m. p. 208-210°. Its mixture with authentic tazettine did not give a melting point depression. $[\alpha]_D$ + 151° (c 0.25; alcohol), R_f 0.49.

The mother liquor after separating the crystalline tazettine was made slightly acid and then evaporated in vacuo. Treatment of the residue with acetone caused it to crystallize. After washing with acetone we obtained isotazettine hydrochloride with m. p. 223-224° and $[\alpha]_D$ + 25.9°.

SUMMARY

1. Together with lycorine and galanthamine, an amorphous base with composition $C_{18}H_{21}O_5N$ was isolated from the bulbs and leaves of Leucojum aestivum, for which the name of isotazettine has been proposed.

2. Isotazettine is apparently an epimeric form of tazettine, into which it is converted when treated with water.

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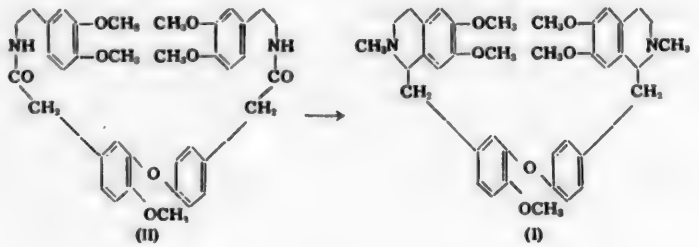
PATHS FOR THE SYNTHESIS OF THE ALKALOID DAURICINE

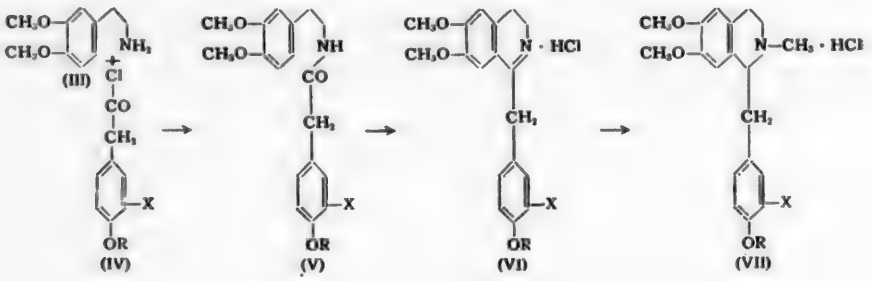
I. N. Gorbacheva, L. A. Nikolaeva and N. A. Preobrazhensky

The synthesis of the methyl ether of the racemic alkaloid dauricine (I) was accomplished [1] by the method of simultaneous closure of the two isoquinoline rings, starting with the corresponding diamide (II), followed by hydrogenation, and then methylation of the secondary nitrogen atom. The reaction of two benzyltetrahydroisoquinoline derivatives (VII)[(a) R = X = H and (b) R = CH_3, X = Br] with the formation of an ether linkage between the benzyl radicals, can serve as a second method for the synthesis of compound (I).



(II) (I)

We synthesized the hydrochloride of 1-(4-benzyloxybenzyl)-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (VII, R = $CH_2C_6H_5$, X = H), the benzyl group of which is easily removed by catalytic hydrogenation, and the hydrochloride of 1-(3-bromo-4-methoxybenzyl)-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (VII, R = CH_3, X = Br) by the scheme



(III) (IV) (V) (VI) (VII)

The chloride of the corresponding phenylacetic acid (IV, R = $CH_2C_6H_5$, X = H and IV, R = CH_3, X = Br) was condensed with β-(3,4-dimethoxyphenyl)ethylamine (III); the obtained amide (V, R = $CH_2C_6H_5$, X = H and V, R = CH_3, X = Br) was cyclized by treatment with phosphorus pentachloride to yield the dihydroisoquinoline derivative (VI, R = $CH_2C_6H_5$, X = H and VI, R = CH_3, X = Br), which was then catalytically reduced and methylated with formalin in the presence of formic acid (VII, R = $CH_2C_6H_5$, X = H and VII, R = CH_3, X = Br). The purpose of the presented synthesis scheme was to obtain the optically active isomers of the methyl ether of the alkaloid dauricine.

EXPERIMENTAL

β-(3,4-Dimethoxyphenyl)ethylamide of 4-benzyloxyphenylacetic acid (V, R = $CH_2C_6H_5$, X = H). A mixture of 2.72 g of 4-benzyloxyphenylacetic acid and 13.3 g of thionyl chloride was heated at the boil for 2 hours. Then the excess thionyl chloride was vacuum-distilled. The residue was dissolved in 20 ml of chloroform and the solution gradually added with constant stirring to a solution of 2 g of β-(3,4-dimethoxyphenyl)ethylamine (III) in 20 ml of chloroform. Simultaneously with this about 20 ml of a 5% potassium hydroxide solution was added at such a rate that a weakly alkaline (to phenolphthalein) reaction medium was constantly maintained. The chloroform layer after separation was washed with 5-10% hydrochloric acid solution, then with water until neutral, and dried over sodium sulfate. The chloroform was removed in vacuo and the residue was rubbed with ether, filtered, and recrystallized from ethyl alcohol. Yield 3.1 g (50.9%). M. p. 124-125.5°.

Found %: C 73.71, 74.27; H 6.26, 6.51; N 3.32, 3.29. $C_{25}H_{27}O_4N$. Calculated %: C 74.07; H 6.66; N 3.46.

β-(3,4-Dimethoxyphenyl)ethylamide of 3-bromo-4-methoxyphenylacetic acid (V, R = CH_3, X = Br. The compound was obtained in exactly the same manner as the preceding, starting with 2.8 g of 3-bromo-4-methoxyphenylacetic acid and 2 g of β-(3,4-dimethoxyphenyl)ethylamine (III). Two recrystallizations from ethyl alcohol gave the compound as colorless crystals. Yield 3.3 g (73.5%). M. p. 111-111.5°.

Found %: C 55.85, 55.98; H 5.09, 5.49; N 3.65, 3.55. $C_{19}H_{22}O_4NBr$. Calculated %: C 55.88; H 5.39; N 3.43.

1-(4-Benzyloxybenzyl)-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (VI, R = $CH_2C_6H_5$, X = H). To a solution of 1.5 g of the β-(3,4-dimethoxyphenyl)ethylamide of 4-benzyloxyphenylacetic acid (V, R = $CH_2C_6H_5$, X = H) in 11 ml of chloroform was gradually added, with stirring and cooling, a solution of 1.56 g of phosphorus pentachloride in 23 ml of chloroform. The reaction mass was allowed to stand at room temperature for three days and then was heated at the boil for 1 hour. The chloroform solution was washed with water, 5% sodium hydroxide solution, 5% hydrochloric acid, again with water until neutral, and dried over sodium sulfate. The solvent was removed in vacuo, while the residue was rubbed in ether and filtered. After 2 recrystallizations from ethyl alcohol and drying in vacuo (at 2-3 mm and 60°) the yield was 1.05 g (67%). M. p. 189-190°.

Found %: C 71.05, 70.51; H 6.29, 6.45; N 3.36, 3.37. $C_{25}H_{26}O_3NCl$. Calculated %: C 70.84; H 6.14; N 3.31.

1-(3-Bromo-4-methoxybenzyl)-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (VI, R = CH_3, X = Br). The conditions used to prepare the compound were the same as the preceding. The starting substance was 1.02 g of the β-(3,4-dimethoxyphenyl)ethylamide of 3-bromo-4-methoxyphenylacetic acid (V, R = CH_3, X = Br). Colorless crystals were obtained after three recrystallizations from ethyl alcohol and drying in vacuo (at 2-3 mm and 60°). Yield 0.45 g (43%). M. p. 191-191.5°.

Found %: C 53.73, 53.57; H 5.07, 5.01; N 3.53, 3.44. $C_{19}H_{21}O_3NClBr$. Calculated %: C 53.45; H 4.92; N 3.28.

1-(4-Benzyloxybenzyl)-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (VII, R = $CH_2C_6H_5$, X = H). A solution of 0.5 g of 1-(4-benzyloxybenzyl)-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (VI, R = $CH_2C_6H_5$, X = H) in 15 ml of anhydrous alcohol was hydrogenated over the platinum catalyst from 0.3 g of platinum oxide for 6 hours at room temperature. The catalyst was filtered, while the alcohol was removed in vacuo in a stream of nitrogen. The residue was dissolved in 50 ml of chloroform, washed with 10% soda solution, then with water, and dried over sodium sulfate. The chloroform was vacuum-distilled, while the isoquinoline base was treated in anhydrous benzene with hydrogen chloride. The isolated 1-(4-benzyloxybenzyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride was again dissolved in 40 ml of chloroform, shaken with 10% soda solution, washed with water, and dried over sodium sulfate. The chloroform was removed in vacuo and the residue was treated with 0.55 ml of 87.8% formic acid and 0.21 ml of 38.4% formalin. The mixture was heated on the water bath for 4.5 hours, whereupon the evolution

of gas bubbles was observed; the mixture after cooling was treated with 20 ml of benzene and then made alkaline by the addition of 5% sodium hydroxide solution. The benzene extract was washed with water until neutral (to phenolphthalein) and then dried over sodium sulfate. Then the benzene solution was shaken with animal charcoal, filtered, and the hydrochloride of the base precipitated by the addition of a benzene solution of hydrogen chloride. The precipitate was washed with ether by decantation until neutral (to Congo) and then dried in vacuo (1-2 mm) for 3 hours at 60°. The compound was obtained as nearly colorless crystals. Yield 0.12 g (22.8%). M. p. 184-186°.

Found %: C 71.11, 71.10; H 6.60, 6.90; N 2.97, 3.07. $C_{28}H_{30}O_3NCl$. Calculated %: C 70.99; H 6.82; N 3.18.

1-(3-Bromo-4-methoxybenzyl)-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (VII, R = CH_3, X = Br). The compound was obtained from 0.25 g of 1-(3-bromo-4-methoxybenzyl-6,7-dimethoxy-3,4-dihydroisoquinoline hydrochloride (VI, R = CH_3, X = Br) by exactly the same procedure used to synthesize the preceding compound. The isolated substance was slightly yellow. Yield 0.1 g (38.4%). M. p. 164-168°.

Found %: C 54.21, 54.75; H 5.89, 5.79; N 2.98, 3.09. $C_{20}H_{25}O_3NClBr$. Calculated %: C 54.24; H 5.65; N 3.17.

SUMMARY

The hydrochlorides of 1-(4-benzyloxybenzyl)-and 1-(3-bromo-4-methoxybenzyl)-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolines were prepared and characterized, as were also a number of the intermediates in their synthesis.

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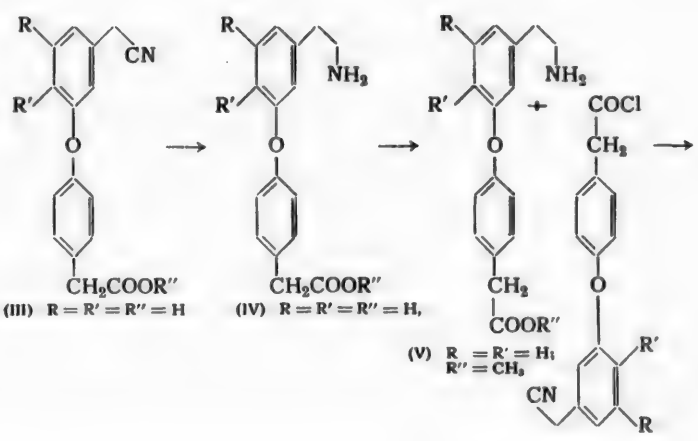
PATHS FOR THE SYNTHESIS OF THE ALKALOID ISOCHONDODENDRINE

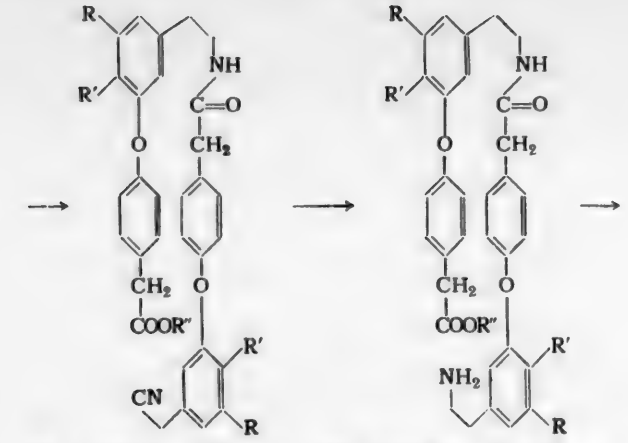
CYCLO {BIS(4-[3-(β-AMINOETHYL)PHENOXY]PHENYLACETYL)}

E. N. Tsvetkov, I. N. Gorbacheva and N. A. Preobrazhensky

Isochondodendrine (I) belongs to the class of macrocyclic bisbenzyltetrahydroisoquinoline alkaloids, compounds that are characterized by possessing various and interesting physiological properties. A scheme for the synthesis of isochondodendrine (I) and its dimethyl ether (II) is proposed in the present paper. The principal step in the indicated scheme is the intramolecular cyclization of amide (VIIIa), which should lead to the formation of the macrocyclic diamide (IXa); the latter through a number of steps can be converted to either isochondodendrine (I) or its dimethyl ether (II). To us the building of the macrocyclic system by intramolecular cyclization seems to be a more rational approach than the use of bimolecular condensations, which have been proposed earlier for the synthesis of similar compounds [1-4].

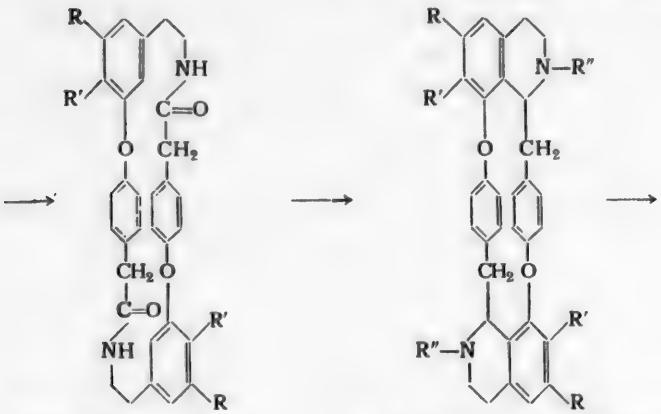
The proposed method finds experimental verification in the synthesis of cyclo {bis(4-[3-(β-aminoethyl)-phenoxy]phenylacetyl} (IX), which was accomplished by the following scheme.





(VI) R = R′ = H; R″ = CH₃
(VII) R = R′ = R″ = H

(VIII) R = R′ = H; R″ = CH₃
(VIIIa) R = OCH₃; R′ = OCH₃ or OCH₂C₆H₅; R″ = CH₃ or H.



(IX) R = R′ = H
(IXa) R = OCH₃; R′ = OCH₃ or OCH₂C₆H₅

(I) R = OCH₃; R′ = OH, R″ = CH₃
(II) R = R′ = OCH₃; R″ = CH₃
(X) R = R′ = R″ = H

The catalytic reduction of 3-cyanomethyl-4'-carboxymethyldiphenyl ether (III) [5] in the presence of skeletal nickel catalyst in aqueous ammonia medium led to 3-(β-aminoethyl)-4'-carboxymethyldiphenyl ether (IV), which was then esterified at room temperature. If the esterification was done hot, a by-product, apparently a polymer, was usually formed, the yield of which increased to 60-70% as the time of heating and concentration of the starting amino acid (IV) were increased. 3-(β-aminoethyl)-4'-carbomethoxymethyldiphenyl ether (V) was acylated with the acid chloride of 3-cyanomethyl-4'-carboxymethyldiphenyl ether. Reduction of the nitrile group in the obtained amide (VI) gave only fair results. A better reduction method proved to be that in which the carbomethoxy group of amide (VI) was selectively saponified with an aqueous alcohol solution of sodium hydroxide at room temperature, and the obtained compound (VII) was reduced as the ammonium salt in the presence of skeletal nickel catalyst and then esterified.

The intramolecular cyclization of amino ester (VIII) was run under conditions of great dilution, with gradual addition of a solution of the amino ester in xylene to a large volume of the same solvent, and with heating to the boil and vigorous stirring. The reaction products were saponified with aqueous-alcoholic alkali at room temperature to remove linear amides as the sodium salts. This treatment lent support to the cyclic nature of the obtained compound.

Recrystallization of macrocyclic diamide (IX) from a mixture of carbon tetrachloride and propyl alcohol gave a stable solvate of the diamide with carbon tetrachloride (4 molecules of the diamide per molecule of carbon tetrachloride). We were unable to remove the solvent even after prolonged (6 hours) heating in vacuo (1 mm) at 140°. The pure compound was obtained by precipitation of the solvate from chloroform with ether and subsequent recrystallization from methyl alcohol. It is possible that carbon tetrachloride was retained by the substance due to the formation of a hydrogen bond between the chlorine atoms and the hydrogen of the amide group.

Cyclization of diamide (IX) by the Bischler-Napieralski method, followed by hydrogenation, gave two compounds with m. p. 225-227° and 121-124°, the apparent structure of which is depicted by formula (X); the existence of two forms is explained by the presence of two asymmetric carbon atoms.

EXPERIMENTAL

3-(β-Aminoethyl)-4'-carboxymethyldiphenyl ether hydrochloride (IV). A solution of 1 g of 3-cyanomethyl-4'-carboxymethyldiphenyl ether (III) [5, 6] in 40 ml of 25% aqueous ammonia was hydrogenated in an autoclave in the presence of 1 g of skeletal nickel catalyst for 2 hours at 100-110° and an initial pressure of 120 atm. The catalyst was separated and washed with 20 ml of water. The filtrate was vacuum-evaporated to dryness, treated with 20 ml of 5% hydrochloric acid, the water distilled off, the dry residue dissolved in 30 ml of methyl alcohol, and then precipitated with 100 ml of ether. The yield of hydrochloride was 1.05 g (91.3%). To remove inorganic impurities the substance was washed with 30 ml of water, then dissolved in 20 ml of methyl alcohol, and precipitated with 100 ml of ether. Colorless crystals were obtained. M. p. 207-209°.

Found %: C 62.76; H 5.84; N 4.76, 4.70. $C_{16}H_{18}O_3NCl$. Calculated %: C 62.44; H 5.89; N 4.55.

3-(β-Aminoethyl)-4'-carbomethoxymethyldiphenyl ether hydrochloride (V). A solution of 1.8 g of ester hydrochloride (IV) in 200 ml of anhydrous methyl alcohol was saturated with dry hydrogen chloride and then allowed to stand for 24 hours. The methanol was removed in vacuo, and the residue was dissolved in 5 ml of methyl alcohol and precipitated with 70 ml of ether. The yield of hydrochloride was 1.4 g (74.3%). M. p. 160-162°. Recrystallization from methyl ethyl ketone gave the compound as colorless crystals; m. p. 163.8-164.8°.

Found %: C 63.50, 63.42; H 6.05, 6.02; N 4.63, 4.52. $C_{17}H_{20}O_3NCl$. Calculated %: C 63.44; H 6.22; N 4.35.

N-{β-[3-(4'-Carbomethoxymethylphenoxy)phenylethyl]}-4"-(3"'-cyanomethylphenoxy)phenylacetamide (VI). A mixture of 1.8 g of ester (III) and 5 ml of thionyl chloride was heated on the water bath for 30 minutes. The excess thionyl chloride was vacuum-distilled, and its remainder was removed by the repeated addition of dry benzene and subsequent removal by distillation; the obtained oily substance was dissolved in 30 ml of anhydrous chloroform. At the same time 1 g of ester hydrochloride (V) was suspended in 40 ml of chloroform and to it was added, with vigorous stirring, 0.85 g of potash in 15 ml of water and a solution of the acid chloride of 3-cyanomethyl-4'-carboxymethyldiphenyl ether, prepared in the manner indicated above. After 20 minutes the organic layer was separated, washed with saturated potash solution then with 5% hydrochloric acid, and dried over sodium sulfate. The residue after removal of the chloroform was dissolved in 3 ml of dioxan and then precipitated with 40 ml of methyl alcohol. Yield of (VI) 1.6 g (93.6%). M. p. 102.8-103.8°.

Found %: C 74.29, 74.23; H 5.72, 5.74; N 5.42, 5.42. $C_{33}H_{30}O_5N_2$. Calculated %: C 74.16; H 5.62; N 5.24.

N-{β-[3-(4'-Carboxymethylphenoxy)phenylethyl]}-4"-(3"'-cyanomethylphenoxy)phenylacetamide (VII). To a solution of 2 g of acetamide (VI) in 10 ml of dioxan was added 10 ml of methyl alcohol and 0.3 g of sodium hydroxide in 2 ml of water. The mixture was allowed to stand at room temperature for 2-3 hours, the solvents removed in vacuo, the residue diluted with 30 ml of water, acidified with 5% hydrochloric acid until weakly acid, and extracted with chloroform. The extract was dried and concentrated in vacuo to give a crystalline residue of (VII), m. p. 128-131°, yield 1.4 g (71.8%). Two recrystallizations from chloroform gave the compound as colorless crystals, m. p. 134-135.5°.

Found %: C 74.25, 73.74; H 5.43, 5.58; N 5.23, 5.26. $C_{32}H_{28}O_5N_2$. Calculated %: C 73.83; H 5.38; N 5.38.

N-{β-[3-(4'-Carbomethoxymethylphenoxy)phenylethyl]}-4"-[3"'-(β'-aminoethyl)phenoxy]phenylacetamide (VIII). a) Hydrogenation on palladium catalyst. To a solution of 1.6 g of acetamide (VI) in a mixture of 40 ml of anhydrous methyl alcohol and 20 ml of dioxan was added 0.5 ml of concentrated sulfuric acid and

the mixture hydrogenated at room temperature and atmospheric pressure in the presence of 0.5 g of palladium black, previously saturated with hydrogen. After 8 hours the amount of hydrogen absorbed was 125 ml at 18° and 735.5 mm (83% of the theoretical). The catalyst was separated, the solution concentrated in vacuo to a volume of 5-6 ml, poured into 100 ml of water, and the precipitate filtered and washed with 50 ml of water. Two recrystallizations from methyl alcohol gave the compound as colorless crystals. Yield of the sulfate of (VIII) 0.4 g (22.7%). M. p. 226.5-227.5°.

Found %: C 67.66, 67.42; H 5.94, 5.68; N 4.85, 4.99. $C_{33}H_{35}O_7N_2S_{1/2}$. Calculated %: C 67.47; H 5.96; N 4.77.

b) Hydrogenation on nickel catalyst. A solution of 0.9 g of acetamide (VII) in 50 ml of anhydrous ammonia-saturated methyl alcohol was hydrogenated in an autoclave in the presence of 0.5 g of skeletal nickel catalyst at 100° and an initial pressure of 100 atm for 3 hours. After cooling the reaction mass the catalyst was filtered and washed thoroughly with 100 ml of anhydrous methyl alcohol, acidified with 1 ml of concentrated sulfuric acid. The ammoniacal filtrate was vacuum-evaporated to dryness, the residue was dissolved in the alcohol used to wash the catalyst, and the mixture was allowed to stand for 24 hours. The solution was concentrated in vacuo to a volume of 8-10 ml and then poured into 100 ml of water. The precipitate was filtered and dried in a vacuum-desiccator. Yield 0.65 g (64.2%). M. p. 200-208°. Two recrystallizations from methyl alcohol gave the compound as colorless crystals. Yield of the sulfate of (VIII) 0.3 g (29.5%). M. p. 226-227°. The mixed melting point with the sulfate of acetamide (VIII), obtained by the first method, was 226-227°.

Cyclo {bis(4-[3-(β-aminoethyl)phenoxy]phenylacetyl)}(IX). A suspension of 0.7 g of the sulfate of acetamide (VIII) in 70 ml of chloroform was shaken in a separatory funnel with 5 ml of methyl alcohol and a solution of 0.15 g of sodium bicarbonate in 30 ml of water. The chloroform layer was separated, dried over sodium sulfate, and mixed with 300 ml of xylene. The solution was concentrated in vacuo to a volume of 200 ml and then added in drops over a period of 20 hours to 1 liter of vigorously stirred boiling xylene. On conclusion of adding the solution the mixture was heated for 10 hours. The xylene was vacuum-distilled, while the residue was dissolved in 20 ml of a dioxan – methanol mixture (1:1), treated with 0.1 g of sodium hydroxide in 2 ml of water, and allowed to stand at room temperature for 2-3 hours. The solvent was removed in vacuo, while the residue was diluted with 30 ml of water and then extracted with chloroform. The extract was dried over sodium sulfate, concentrated to a volume of 10-15 ml, and poured into 150 ml of carbon tetrachloride. The precipitate was filtered. Yield 0.13 g (21.4%). M. p. 192-200°. Three recrystallizations from a mixture of propyl alcohol and carbon tetrachloride (1:1) gave the compound as colorless crystals. The substance tenaciously retains carbon tetrachloride, which could not be removed even on prolonged (6-7 hours) heating in a vacuum of 1 mm and a temperature of 140°. Yield 0.024 g (3.95%). M. p. 204-205°.

Found %: C 70.46, 69.69; H 5.22, 5.16; N 4.82, 5.12; Cl 6.25, 5.80. $C_{32}H_{30}O_4N_2 \cdot {}^1/_4CCl_4$. Calculated %: C 70.51; H 5.51; N 5.14; Cl 6.52.

The carbon tetrachloride was removed by precipitating the obtained compound from chloroform with ether, followed by recrystallization from methyl alcohol. The obtained substance (IX) melted at 185-187°.

Found %: C 75.82; H 5.88; N 5.25, 5.18. $C_{32}H_{30}O_4N_2$. Calculated %: C 75.89; H 5.93; N 5.53.

A solution of 0.07 g ($1.38 \cdot 10^{-4}$ mole) of cyclo {bis(4-[3-(β-aminoethyl)phenoxy]phenylacetyl)} (IX) in 10 ml of anhydrous chloroform was mixed with 0.15 g ($7.2 \cdot 10^{-4}$ mole) of phosphorus pentachloride in 10 ml of anhydrous chloroform. The solution was allowed to stand at room temperature for 3 days, then heated at the boil for 1 hour, cooled, washed with 10% sodium hydroxide solution, shaken with 5 ml of 2% hydrochloric acid, dried over sodium sulfate, and poured into 100 ml of ether. A light yellow amorphous substance was obtained. Picrolonate, m. p. 124-130°.

Found %: C 62.42; H 4.75. $C_{52}H_{42}O_{12}N_{10}$. Calculated %: C 62.52; H 4.21.

Hydrogenation of the cyclization product of diamide (IX) in the presence of platinum black (from PtO_2) gave two compounds (X) with m. p. 225-227° and 121-124°.

SUMMARY

The synthesis of cyclo{bis(4-[3-(β-aminoethyl)phenoxy]phenylacetyl)} was accomplished through a number of steps.

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COMPLEX COMPOUNDS OF $SnCl_4$, $SnBr_4$ and $TiCl_4$ WITH CINEOLE

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Complex compounds of $SnCl_4$, $SnBr_4$ and $TiCl_4$ with organic oxides have hardly been studied. Compounds of $SnCl_4$ and $SnBr_4$ with dioxan [1], and of $SnCl_4$ with lactones [2] of general formula $SnX_4 \cdot 2A$, have been described in the literature.

It seemed of interest to us to make a systematic study of the complex compounds of Sn^{+4} and Ti^{+4} with organic compounds containing the $-COC-$ group. For our study we selected cineole, found in many essential oils. A study of the complex compounds of the halides of tin and titanium with cineole was also of interest to us in connection with a search for a method for the quantitative determination of cineole.

EXPERIMENTAL

To obtain the complex compounds we prepared mixtures of $SnCl_4$, $SnBr_4$ and $TiCl_4$ with cineole in definite molecular proportions. For the reactions, accompanied by much heat evolution, the mixing of the components was done in inert solvents.

The composition of the complex compounds was established analytically and by the cryoscopic titration method [3, 4]. Tin and titanium were determined as SnO_2 and TiO_2. The halides were determined by the Volhard method. The cryoscopic measurements were run in a Beckman apparatus with electromagnetic stirrer. The obtained data were used to construct the diagrams showing the relationship between the melting point depression (or molecular weight) and the composition, expressed in mole percent.

Stannic chloride was prepared by the earlier described method [5]; the fraction with b. p. 109° (694.5 mm) was collected and sealed in ampuls. The stannic bromide was purified by repeated distillation. For our work we took the fraction with b. p. 198° at 695 mm; m. p. 31.0°. This fraction was redistilled and sealed in ampuls. The titanium tetrachloride was redistilled several times. The fraction with b. p. 132.5° (699.4 mm) was sealed in ampuls. The cineole, isolated from wormseed oil by treatment with resorcinol [6], after distillation was purified by fractional freezing; its m. p. 0.7° (from the literature, m. p. 1.5°). The benzene of "cryoscopic" grade was purified further in the usual manner and then subjected to fractional freezing; m. p. 5.5°. The c. p. acetic acid was first purified by freezing and then distilled; m. p. 16.2°.

Complex Compound of Stannic Chloride with Cineole

The mixing of stannic chloride with cineole is accompanied by much heat evolution. To avoid decomposition of the complex compound we slowly added the solution of cineole in benzene (calculated on the basis of 1 mole of stannic chloride per mole of cineole, and 1 mole of stannic chloride per 2 moles of cineole) in drops to an ice-cooled solution of stannic chloride in benzene. The obtained solutions were transferred to porcelain dishes, which were placed in a vacuum-desiccator over P_2O_5. Evaporation of the benzene contained in the porcelain dishes left colorless crystalline precipitates. The precipitate obtained from the 1:1 mixture, which proved difficult to dry and fumed in the air, was washed by decantation with small portions of cold benzene.

Analysis of the precipitates that deposited from the 1:2 mixture gave the following results:

Found %: Sn 19.70, 20.37, 19.79, 20.15; Cl 24.08, 23.99, 24.11, 23.93. $SnCl_4 \cdot 2C_{10}H_{18}O$. Calculated %: Sn 20.86; Cl 24.93.

The precipitates that deposited from the 1:1 mixture showed the following analysis data.

Found %: Sn 22.31, 21.82, 22.10; Cl 25.97, 25.98, 26.04. $SnCl_4 \cdot C_{10}H_{18}O$. Calculated %: Sn 28.62; Cl 34.19.

As a result, the amount of tin and chlorine contained in the precipitates obtained from both the 1:1 and 1:2 mixtures corresponds to the compound $SnCl_4 \cdot 2C_{10}H_{18}O$. A tin and chlorine content higher than theory for a 1:2 compound in the precipitate isolated from the 1:1 mixture is probably due to the fact that we were unable to completely wash out the excess stannic chloride from the precipitate.

The molecular weight of the obtained substance was determined cryoscopically. The results of two determinations are given below:

1) 0.6031 g of substance, dissolved in 12.77 g of CH_3COOH, lowered the freezing point 0.340°. From this M = 542.

2) 1.2425 g of substance, dissolved in 12.77 g of CH_3COOH, lowered the freezing point 0.705°. From this M = 538.

The molecular weight, calculated from the formula $SnCl_4 \cdot 2C_{10}H_{18}O$, is equal to 569.01; calculated from the formula $SnCl_4 \cdot C_{10}H_{18}O$ it is equal to 414.77. Consequently, the cryoscopic data support the formation of the complex $SnCl_4 \cdot 2C_{10}H_{18}O$.

The results of the direct and reverse cryoscopic titration of $SnCl_4$ and $C_{10}H_{18}O$ are shown in Fig. 1. When cineole is added to a benzene solution of stannic chloride the magnitude of depression remains constant up to 66 mole % of cineole, after which an increase in the depression is observed. When the order of adding the reagents is reversed the depression decreases down to 66 mole % of cineole, and with further addition of the reagent an increase in the depression occurs; at the minimum point the value of the depression is equal to one half of the original. The shape of the curves showing the relationship between the depression and the molecular ratio of the components indicates that an undissociated compound with a 1:2 composition is formed. The molecular weight–composition diagram (Fig. 1) of the system $SnCl_4$–$C_{10}H_{18}O$ has a singular point, which is found at 66 mole % of cineole and a molecular weight of 589. This diagram, as does the preceding, shows the formation of compound $SnCl_4 \cdot 2C_{10}H_{13}O$.

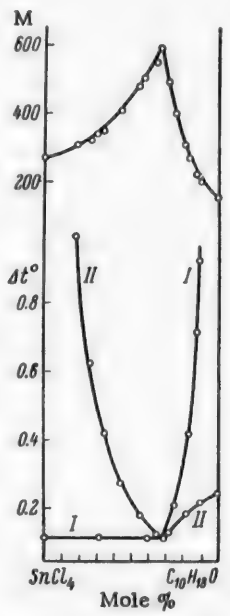

Fig. 1. Freezing point depression–composition and molecular weight–composition diagrams of the system $SnCl_4$–$C_{10}H_{18}O$. I) cineole added, II) stannic chloride added.

The complex compound $SnCl_4 \cdot 2C_{10}H_{18}O$ is a colorless crystalline substance, which rapidly turns red in the air and deliquesces; it is soluble in benzene, acetic acid and other organic solvents; it sublimes without melting.

Complex Compound of Stannic Bromide with Cineole

When stannic bromide is mixed with cineole the formation of a precipitate is observed, accompanied by a small heat effect. We prepared mixtures of stannic bromide and cineole with a variable stoichiometric composition (1:1) and (1:2) in the absence of a solvent. The 1:2 mixture crystallized completely; the 1:1 mixtures, together with a precipitate, contained a heavy fuming liquid. The slight warming of these mixtures to about 35° gave a sublimate of colorless lustrous needles.

Analysis of the sublimate obtained from the 1:2 mixture is given below.

Found %: Sn 15.47, 15.51, 15.40; Br 42.34, 42.65, 42.63. $SnBr_4 \cdot 2C_{10}H_{18}O$. Calculated %: Sn 15.89; Br 42.80.

Analysis of the sublimate obtained from the 1:1 mixture gave the following results:

Found %: Sn 15.45, 15.17; Br 42.25, 42.59. $SnBr_4 \cdot C_{10}H_{18}O$. Calculated %: Sn 20.03; Br 53.95.

The analysis data show that the same substance, namely $SnBr_4 \cdot 2C_{10}H_{18}O$, is formed when the components are mixed in variable stoichiometric proportions.

Cryoscopic determination of the molecular weight of the sublimed substance gave the following results:

1) 0.1871 g of substance dissolved in 11.29 g of CH_3COOH lowered the freezing point 0.090°. From this M = 718.

2) 0.2452 g of substance dissolved in 11.29 g of CH_3COOH lowered the freezing point 0.115°. From this M = 723.

The molecular weight, calculated from the formulas $SnBr_4 \cdot 2C_{10}H_{18}O$ and $SnBr_4 \cdot C_{10}H_{18}O$, is equal to 746.84 and 592.60, respectively. Consequently, the cryoscopic data support the formation of the complex $SnBr_4 \cdot 2C_{10}H_{18}O$.

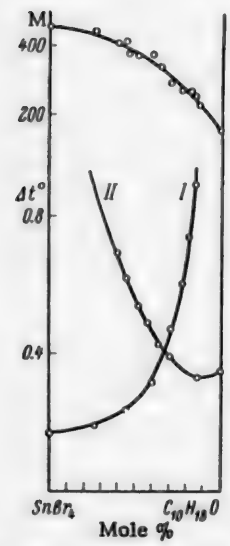

Fig. 2. Freezing point depression–composition and molecular weight–composition diagrams of the system $SnBr_4-C_{10}H_{18}O$. I) cineole added, II) stannic chloride added.

The results of the cryoscopic titration of the system $SnBr_4-C_{10}H_{18}O$ are shown in Fig. 2. When cineole is gradually added to a benzene solution of stannic bromide the depression increases slowly at first, and then, beginning with 60 mole % of cineole, a sharp increase in the depression is observed. When the reagents are added in the reverse order the depression decreases at first, and then, beginning with 80 mole % of cineole, it increases sharply. The shape of the curves for the change in the freezing point depression of the system $SnBr_4-C_{10}H_{18}O$, and also the molecular weight–composition diagram, indicate the presence of chemical reaction between the components. However, these diagrams do not give an indication of the composition of the compound formed, since in benzene solution the reaction does not go to completion.

The complex compound $SnBr_4 \cdot 2C_{10}H_{18}O$ is a colorless crystalline compound, readily soluble in benzene and other organic solvents. It rapidly turns red in the air and deliquesces.

The ability of this compound, having a large molecular weight, to sublime at a temperature of only 35° deserves special consideration. The components of the system (stannic bromide and cineole) are slightly volatile substances that boil at high temperatures. For this reason the vapor pressure diagram of the system should have a maximum, corresponding to the 1:2 composition. The presence of a substantial positive deviation on diagrams of this type is a rare case.

The low sublimation temperature causes us to postulate a strictly symmetrical molecular structure for the compound. However, the dipole moment of $SnBr_4 \cdot 2C_{10}H_{18}O$ is equal to 3.88 debyes [7].

Complex Compound of Titanium Tetrachloride with Cineole

An orange-red precipitate is formed when benzene solutions of titanium tetrachloride and cineole are mixed; the reaction is accompanied by much heat evolution. Mixtures of $TiCl_4$ and cineole were prepared in the molecular proportions 1:1 and 1:2.

We were unable to analyze the obtained compound due to the exceeding ease with which it hydrolyzed. The composition of this compound was established from a cryoscopic study of the system $TiCl_4-C_{10}H_{18}O$.

The depression of the freezing point was measured only in the case of adding cineole to a benzene solution of titanium tetrachloride. A known weight of $TiCl_4$ was placed in a thick-walled glass ampul, which was broken in the cryoscope. When cineole was gradually added to a benzene solution of titanium tetrachloride

the depression remained practically constant up to approximately 60 mole % of cineole, and then a sharp increase in it was observed (Fig. 3). The constancy of the depression indicates that in the addition of cineole to a benzene solution of titanium tetrachloride one molecule of the compound is formed in solution for each molecule of $TiCl_4$ that disappears. On the molecular weight–composition diagram a maximum is found at 35 mole % $TiCl_4$ and a molecular weight equal to 450. This corresponds to the compound $TiCl_4 \cdot 2C_{10}H_{18}O$ (formula molecular weight 489.73). The compound is an orange-red powderlike substance that hydrolyzes with decomposition when stored. It is soluble in benzene and other organic solvents.

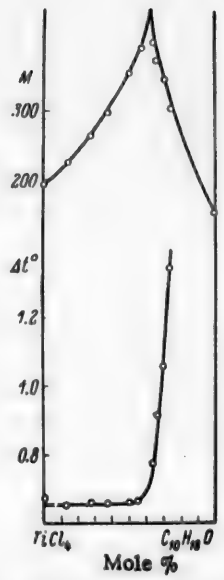

Fig. 3. Freezing point depression–composition and molecular weight–composition diagrams of the system $TiCl_4$–$C_{10}H_{18}O$.

SUMMARY

1. The complex compounds $SnCl_4 \cdot 2C_{10}H_{18}O$, $SnBr_4 \cdot 2C_{10}H_{18}O$ and $TiCl_4 \cdot 2C_{10}H_{18}O$ were obtained.

2. It was found that the complex compound $SnBr_4 \cdot 2C_{10}H_{18}O$ possesses unusual properties. This compound, having a high molecular weight (746.8), sublimes at a temperature of about 35°.

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AN APPROXIMATE METHOD FOR CALCULATION OF MELTING POINTS IN HOMOLOGOUS SERIES

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The melting point is an important physical constant that serves to characterize, identify and determine the purity of organic compounds. If the simplicity of the measurement method (determined by a practical independence of the $t_{m.p.}$ on the pressure and the elimination of superheating), the need of having only a small amount of compound, and also the stability of most substances at $t \leq t_{m.p.}$ is taken into consideration, then it becomes clear why the melting point is usually the first specific property used to study a newly synthesized compound.

As a rule, for the higher members of a homologous series the values of $t_{m.p.}$ are not known, and if they have been determined, then only with a very small accuracy (for most studied substances with an error of the order of 1°). Only for the n-alkanes, up to approximately C_{40}, are they known with an error of less than 1°; to them perhaps could also be added many 1-alkenes and n-monoalkylcyclohexanes. Only for individual compounds with a high molecular weight did the purity of the studied specimens (~99.9%) assure a determination of the $t_{m.p.}$ with an accuracy of the order of 0.1-0.01° [2, 3].*

At the same time a calculation of the melting point is difficult. This value is not additive; in addition, the same as is true for some other properties of crystalline compounds, it suffers a peculiar variation in most homologous series.

If several of the first homologs are discarded, then it becomes possible to speak of four types of melting point changes. These types are shown in Fig. 1 on individual examples. Dibasic dicarboxylic acids belong to the homologous series in which the sequence of change in the melting points corresponds to line I; monobasic carboxylic acids, mercaptans (1-alkylthiols) and diamines belong to type II. N-Alkanes, 2-alkanethiols, saturated monohydric alcohols, n-monoalkylnapthalenes, 1-alkynes and n-monoalkylcyclopentanes can be regarded as belonging to the homologous series in which $t_{m.p.}$ constantly increases along a line of type III with increase in the molecular weight. Within the limits of experimental error an approximately monotonic course of the melting point (line IV) is observed for n-monoalkylcyclohexanes, n-monoalkylbenzenes, 2-methyl-1-alkenes and ketones $CH_3-CO-C_nH_{2n+1}$.**

It is possible that for some homologous series the error of the experimental data is commensurate with the deviation from a smooth curve, which makes it difficult to classify them with the proper group. The 1-alkenes belong to such compounds. If it is assumed that oscillation of the melting points is a general property of homologous series, then it follows that groups that had been classified as belonging to type IV, should be added to type III.

A periodicity in the change in melting points, first revealed by Bayer [5], subsequently served as the subject of a number of investigations.*** Possible explanations of this phenomenon were also proposed in some of

*Only in a single investigation, devoted to a study of the thermodynamic properties of 1,3-butadiene [1], due to the fact that the purity of the compound was raised to 99.9998% , did it prove possible to obtain very accurate results (in such cases it is necessary to introduce a correction for the barometric pressure).

** The $t_{m.p.}$ values for the hydrocarbons were copied from either [2] or [3], and for the other organic compounds mainly from [4].

***It is necessary to mention the work of B. V. Nekrasov [6]. A summary of the studies devoted to this problem can be found in [7]; (see also [8]).

these investigations. Other studies contained new experimental data, supporting the nonmonotonic course of the $t_{m.p.}$ values.

The purpose of the present paper is to investigate one possible way of calculating the $t_{m.p.}$ values.

Molecules with an even number of CH_2 groups in the hydrocarbon chain are similarly constructed; molecules with an odd number of CH_2 groups are in turn similarly constructed. In particular, this appears in the fact that if we were to connect on each of the lines in Fig. 1 the points with an even and with an odd value of n we would obtain two smooth curves (in all of the cases where the $t_{m.p.}$ values are sufficiently reliable). Consequently, a given homologous series could be regarded as consisting as it were of two groups of compounds. This permits recommending one of the earlier described methods of making a comparative calculation of various properties [9] for calculating the melting points. The approximate linear equation

$$G_{II} \approx AG_I + B, \tag{1}$$

corresponds to this method in which G_I and G_{II} are the values of a given property in two series of related compounds, and A and B are constants.

For the particular case of melting points, equation (1) assumes the form of the equation

$$(t_{m.p.})_{odd} \approx A(t_{m.p.})_{even} + B, \tag{2}$$

in which $(t_{m.p.})_{even}$ and $(t_{m.p.})_{odd}$ are the melting points (at constant pressure) of adjacent homologs, having respectively an even and an odd number of carbon atoms, and A and B are constants for a given homologous series. Coefficient A in this equation is always different from unity, since the oscillation of the melting points in any homologous series should diminish with increase in the molecular weight (see, for example, Fig. 1).

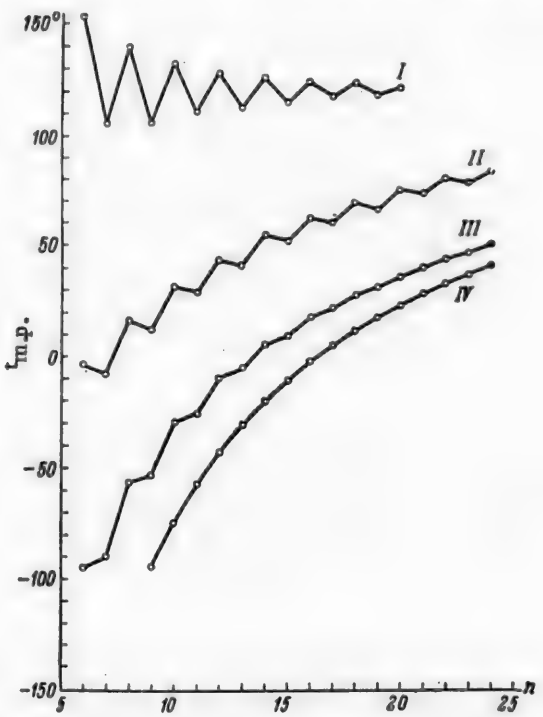

Fig. 1. Relationship between the melting point ($t_{m.p.}$) and the number of carbon atoms (n) in some homologous series. I) Dibasic carboxylic acids; II) monobasic carboxylic acids, III) n-alkanes; IV) n-monoalkylcyclohexanes.

Equation (2) also extends to the case of a practically monotonic change in $t_{m.p.}$ with $\underline{n}$ (Fig. 1; type IV), which can be regarded as the limit in the sequence I → II → III → IV, where the lines of the even and odd $\underline{n}$ merge into one at all values of $\underline{n}$.•

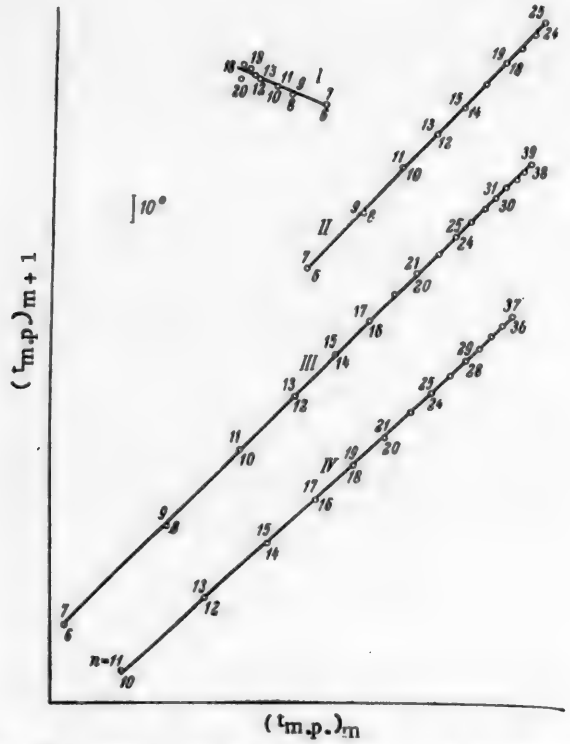

Fig. 2. Interrelationship of the melting points of the members of some homologous series, containing an even (m) and an odd (m+1) number of carbon atoms $\underline{n}$ in the molecule (the numbers denote the number of CH_2 groups in the hydrocarbon chain of the corresponding compound). I) Dibasic carboxylic acids; II) monobasic carboxylic acids; III) n-alkanes; IV) n-monoalkylcyclohexanes (for convenience the lines were arranged arbitrarily).

As can be seen from Fig. 2, equation (2) describes the experimental data with satisfactory accuracy, in which connection the character of the alternation in the melting points is not reflected on the accuracy of the results.•• If we limit ourselves to a comparatively small number of the higher homologs, then it becomes possible to obtain extremely accurate results. Thus, with the aid of the equation

$$(t_{m.p.})_{m+1} \approx 0.945\,(t_{m.p.})_m + 5.6 \qquad (3)$$

• As a known, a monotonic course of the melting points is observed in the series of inorganic compounds, which also leads to an equation of the (2) type (see, for example, [10]).

•• In evaluating the accuracy of equation (2) it should be remembered that the reliability of the $t_{m.p.}$ values in the dibasic acid series is quite small for most of the compounds (different recommendations differ from each other by 1 to 3°).

(where m is an even number) the interrelationship between the melting points of n-alkanes with n = 19 to 39 is described by an average deviation of 0.08° from the data recommended in the literature [2] as being the most reliable.

To increase the reliability of the results of calculating the melting points by equation (2) it is necessary to carry out the operation twice, taking the pairs $t_{m+1} - t_m$ and $t_{m-1} - t_m$, since the curvature of the line $(t_{m.p.})_{odd} - (t_{m.p.})_{even}$, quite perceptible when many compounds are embraced, is opposite in sign for these two comparisons. In addition, in the general case a basis does not exist for giving preference to one of two possible sequences in comparing the melting point values. The average of the obtained values is taken as the sought $t_{m.p.}$.

The data presented in the Table illustrate the accuracy of the calculations using Equation (2) on the example of some of the higher n-monoalkylcyclohexanes. Here the experimental values are compared with the calculated, using the equations

$$(t_{m.p.})_{m+1} \approx 0.91\,(t_{m.p.})_m + 7.5, \quad (4)$$

$$(t_{m.p.})_{m-1} \approx 1.10\,(t_{m.p.})_m - 8.4. \quad (5)$$

The $(t_{m.p.})_m$ values were copied from [2]. As can be seen from the data in the Table, the average deviations of the data, calculated using Equations (4) and (5), are respectively 0.5 and 0.4°. If we take the average values of the $t_{m.p.}$ calculated by these equations, then the error becomes less than 0.1°. Taking into consideration the fact that the inaccuracy of the experimental data also reflects on the calculation results, it must be acknowledged that these results are entirely satisfactory.

Melting Points of Some of the Higher n-Monoalkylcyclohexanes

n	$t_{m.p.}$ based on experimental data [2]	$t_{m.p.}$ based on equation (4)	$t_{m.p.}$ based on equation (5)	Average value of $t_{m.p.}$	$\Delta t_{m.p.}$
11	−57.5	−60.5	−55.7	−58.1	−0.3
13	−30.5	−31.6	−30.1	−30.9	−0.4
15	−10.2	−10.4	−10.3	−10.4	−0.2
17	5.8	5.9	+ 5.4	+ 5.7	−0.1
19	18.5	18.9	18.0	18.5	0.0
21	29.3	29.3	28.6	29.0	0.0
23	37.8	38.1	37.4	37.8	0.0
25	45.2	45.4	44.9	45.2	0.0
27	51.5	51.6	51.4	51.5	0.0
29	57.0	57.0	57.1	57.1	0.1
31	61.9	61.6	61.9	61.8	−0.2
33	66.1	65.7	66.4	66.1	0.0
35	69.9	69.4	70.4	69.9	0.0
37	73.3	72.7	73.9	73.3	0.0

Together with a similarity of the even and odd members of a given homologous series it is also possible to speak of a similarity of the even (or correspondingly odd) members of different homologous series. In principle this substantially expands the scope of the calculation method, since it permits employing Equation (1) in the form of the equation

$$(t_{m.p.})_{II} \approx A\,(t_{m.p.})_I + B, \quad (6)$$

in which $(t_{m.p.})_I$ and $(t_{m.p.})_{II}$ are the melting points (at a given pressure) of the corresponding compounds in two homologous series.

It is understood that with the aid of this equation it is also possible to compare the melting points of the compounds of one homologous series with an even number of carbon atoms with the melting points of the compounds of another homologous series with an odd number of carbon atoms. Consequently, in contrast to Equation (2), when using Equation (6), it is expedient in the general case to proceed not from the values of n, but from the number of CH_2 groups in the molecule of the compound. From Fig. 3 it can be seen that with a different course of the $t_{m.p.}$ in the compared series (line A) the points for the even and odd members of the series are located on two lines; with a similar course of the $t_{m.p.}$ (B) these lines approach each other, but still the distance between them exceeds the experimental error, and finally, for the case where the relationship $t_{m.p.} = \varphi(n)$ is practically the same for both series, i.e., it is expressed by smooth curves, the lines $t_{II} - t_I$ practically merge into one (C). As a result, in the last case the method of making a comparative calculation of various properties in the form in which it was used earlier [9], can also be used for the calculation of melting points. In the remaining cases it is necessary to use it in the modified form described above, conditioned by the nature of the course of the melting points in the homologous series.

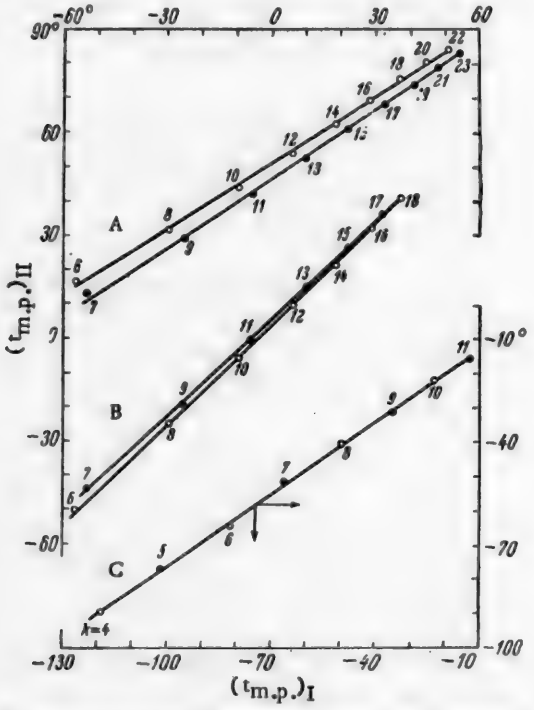

Fig. 3. Interrelationship of melting points. A) n-Alkanes and monocarboxylic acids; B) n-alkanes and 1-alkynes; C) 1-alkenes and 2-methylalkenes (the numbers denote the number of CH_2 groups in the hydrocarbon chain of the corresponding compound).

Since the specific nature of each homologous series in a group of several related series will decline with increase in n, then for large values of n it is possible to assume an approximate agreement in the course of the $t_{m.p.}$ values, discussed in the form corresponding to Equation (2). This means that the values of coefficients A and B in Equation (2) will be practically independent of the type of homologous series, i.e., Equations (2) and (6) will coincide. This argument is supported by Fig. 4, where it can be seen that the melting points of the higher homologs of various series of hydrocarbons lie as a first approximation on a common straight line which corresponds to the approximate equation

$$(t_{m.p.})_{k+1} \approx 0.935\,(t_{m.p.})_k + 5.6. \qquad (7)$$

The greatest deviations are shown by the hydrocarbons of those homologous series for which $t_{m.p.}$ values are known with an accuracy of 1° [2].

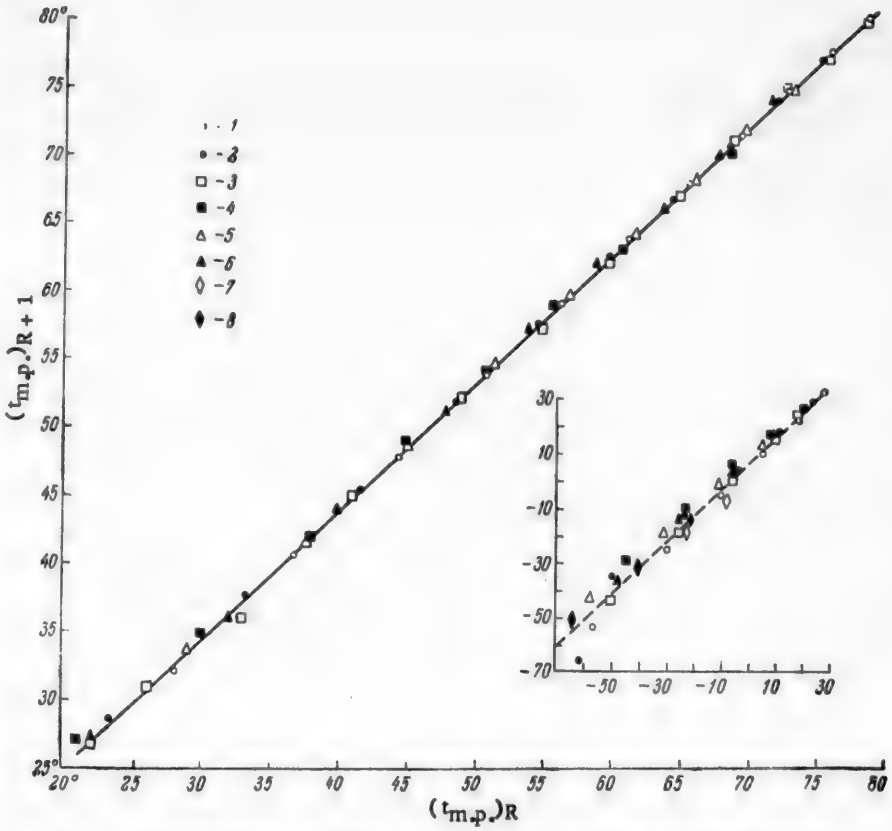

Fig. 4. Interrelationship of melting points of higher members of various homologous series, containing an even (k) and an odd (k+1) number of CH_2 groups in the hydrocarbon chain. 1) n-Alkanes; 2) 1-alkenes; 3) 1-alkynes; 4) n-monoalkylcyclopentanes; 5) n-monoalkylcyclohexanes; 6) n-monoalkylbenzenes; 7) n-monoalkylnaphthalenes; 8) 2-methyl-1-alkenes.

In conclusion we will mention that the possibilities of using a method of comparative computation, and in particular Equation (2), for calculating the melting points of unstudied compounds and making the insufficiently reliable values of these terms more precise, are limited at the present time by the paucity and insufficient accuracy of the experimental data. For most homologous series the melting points are known accurately for the first 5-6 members of the series, i.e, exactly for those compounds for which a correct alternation of the values of the examined property in molecules with an even and odd number of CH_2 groups, making it possible to use Equations (2) and (6), has not yet appeared. However, it is important to emphasize that a method of comparative computation permits organizing an experiment in such manner that, having measured a comparatively small number of values, it becomes possible to obtain the others by calculation. Adding to the fund of data on melting points is of interest not only in itself, but also for an understanding of the nature of solid and liquid states, and in particular, for disclosing the relationship between the melting point and molecular structure.

SUMMARY

To calculate the melting points in homologous series, a method was proposed based on a comparison of the melting points of compounds with an even and odd number of carbon atoms in the molecule.

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MECHANISM OF FORMATION OF GUANIDINE CARBONATE FROM CYANOGUANIDINE, AMMONIUM BICARBONATE, AND AMMONIA IN AQUEOUS SOLUTION

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Due to its great reactivity, guanidine carbonate finds extensive use in industrial organic synthesis. At the present time the simplest and most economical method for its preparation is to heat cyanoguanidine with ammonium bicarbonate in concentrated ammonia solution at 126° at a pressure of 20-22 atm [1]. The by-products of the reaction are ammeline and ammelide, and melamine and urea. Data dealing with the mechanism of guanidine carbonate formation under these synthesis conditions have not been published in the literature up to now.

The formation of guanidine carbonate can proceed by two routes: first, through biguanide, by analogy with the mechanism for the formation of other guanidine salts by the fusion of cyanoguanidine with the corresponding ammonium salts [2, 3], and second, through guanylurea, by the Davis method [4]. In the last case it is possible for the guanylurea to subsequently undergo ammonolysis with the formation of guanidine and urea in equimolar amounts. A second possible path for the formation of urea is its preparation from ammonium bicarbonate [5].

The purpose of the present investigation was to study the kinetics and mechanism of the reaction for the formation of guanidine carbonate in the temperature interval 100-150°.

EXPERIMENTAL *

The kinetics of the formation of guanidine carbonate was studied in steel autoclaves, each with a capacity of 12 ml. To avoid contamination of the synthesis product by autoclave corrosion products the reaction mixture was placed in a glass test tube which was inserted in the autoclave. When the method was checked in the Fundamental Organic Synthesis Laboratory of the Gorki Polytechnic Institute it was established that the optimum molar ratio of cyanoguanidine to ammonium bicarbonate is 1 : 1.66. Into each autoclave was charged a mixture of 1 g of cyanoguanidine, 1.4 g of ammonium bicarbonate, 2.5 ml of water and 2.3 ml of liquid ammonia. Five of the loaded autoclaves were placed in a thermostat, where the desired temperature was maintained with an accuracy of ±1°, and then removed from the thermostat at the end of definite time intervals. After removal from the thermostat the autoclaves were cooled under a stream of tap water. To check on the airtightness of the autoclaves the latter were weighed prior to and after experiment. The obtained product, appearing as white crystals with a colorless solution over them, was extracted from the autoclave, dried at 30-40° until the odor of ammonia had disappeared, then dissolved in 100 ml of distilled water, and acidified with 2 N acetic acid; the mixed precipitate, insoluble in water, was filtered and dried at 110° to constant weight. The solution was transferred to a 250 ml volumetric flask and the amount of biguanide, guanylurea, guanidine, melamine and cyanoguanidine in it determined. In addition, the amount of urea was determined in the synthesis product obtained at 130°. The amount of biguanide was determined by the Garby method [6], made more precise by us; the amount of cyanourea was determined by the Garby method [7]; the amount of guanidine was determined by the picrate method of Vozarik [8]; the amount of melamine was determined by the cyanurate method [9]; the amount of urea was determined by the urease method of Marshall [10]; and the amount of cyanoguanidine was determined by the Harger–Buchanan method [10, 11].

The kinetics of the reaction was studied at 100, 110, 120, 130, 140 and 150°. Each experiment was run for 4 hours.

* Student L. M. Polyaninova participated in the experimental portion of this study.

The obtained results are plotted on the graph and given in the table. We calculated the theoretical yield of guanidine in accordance with the reaction mechanism established below for the formation of guanidine carbonate through biguanide.

As can be seen from the graph (see Figure), at all of the investigated temperatures guanidine content in the synthesis product shows constant increase with increase in heating time at a constant temperature. The most rapid formation of guanidine is observed in the first phase of the reaction. The maximum amount of guanidine obtained is 40% of the theoretical yield. With elevation of the temperature the amount of guanidine in the product keeps increasing at a constantly more rapid rate; the influence of temperature elevation on the formation rate of guanidine is especially great in the temperature interval 120-130° during the first two hours of heating.

Amount of Water-Insoluble Compounds, Cyanoguanidine and Urea in the Product Obtained in the Synthesis of Guanidine Carbonate in the Temperature Interval 100-150° with Varying Times of Heating

Time of heating (hours)	Water-insoluble compounds (g)						Cyanoguanidine (g)						Urea (g)
	100°	110°	120°	130°	140°	150°	100°	110°	120°	130°	140°	150°	130°
0.5	0.127	0.099	0.048	0.273	0.140	0.026	—	—	—	—	—	—	0.355
1.0	0.282	0.216	0.079	0.329	0.220	0.179	0.560	0.634	0.703	0.300	0.215	0.275	0.260
2.0	0.282	0.278	0.101	0.354	0.281	0.184	0.545	0.525	0.525	—	0.184	—	0.218
3.0	0.284	0.281	0.132	0.366	0.310	0.188	0.481	0.427	0.494	0.185	0.165	0.125	0.161
4.0	0.323	0.282	0.201	0.377	0.324	0.222	—	—	—	0.121	—	0.104	0.102

As can be seen from the data in the Table, at all of the investigated temperatures the amount of compounds in the product, insoluble in water but soluble in alkali (ammeline and ammelide), increases rapidly at the start with increase in the time of heating, and then after 1 hour of heating either remains constant or increases very slowly. The amount of these compounds in the product shows great variation when the individual syntheses are reproduced. The amount of urea in the synthesis product at 130° increases rapidly at first with increase in the time of heating, and then begins to fall; such a change in the amount of urea can be explained by the fact that the urea formed during heating of the reaction mixture, subsequently suffers hydrolysis with the formation of ammonia and carbon dioxide [12]. At each of the investigated temperatures the amount of unreacted cyanoguanidine in the product shows constant decrease with increase in the time of heating. The transformation rate of cyanoguanidine is especially great in the first phase of the reaction, after which its amount decreases at a uniform rate. Analysis of the obtained samples revealed that melamine was present in amounts not exceeding 0.05 g in the samples obtained at 100, 120 and 130°. Biguanide and guanylurea were not found in any of the obtained samples. By means of preliminary experiments it was shown that biguanide and guanylurea are also absent in the products obtained in the synthesis of guanidine carbonate at 100, 110, 120 and 130°, with a heating time of 15 minutes in all cases.

In order to study the mechanism of the reaction for the formation of guanidine carbonate we ran the synthesis of the latter in the presence of copper sulfate, as being a compound that forms characteristic precipitates with biguanide and with guanylurea, insoluble in water and in alkalies. A mixture of 16 g of cyanoguanidine, 24 g of copper sulfate, 22.4 g of ammonium bicarbonate, 40 ml of distilled water and 36.8 ml of liquid ammonia was charged into a 300 ml autoclave; the autoclave was heated in an oil bath to 105° and kept at this temperature for 10 hours. The obtained product contained a crystalline precipitate of a bright pink, copper compound. Depending on the nature of the intermediate reaction product in the formation of guanidine carbonate the precipitate should have contained either copper biguanide $Cu(C_2H_6N_5)_2$ [13] or copper guanylurea $Cu(C_2H_5ON_4)_2$ [14, 15].

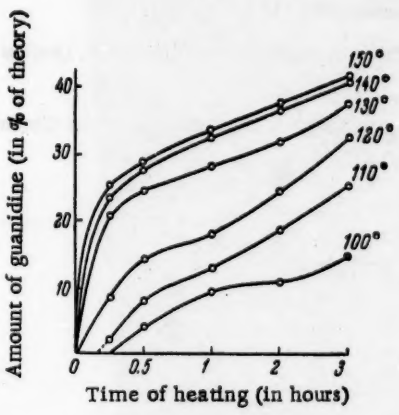
A direct quantitative analysis of the copper compound presented great difficulties: first, the compound contained sulfuric acid, the amount of which, as experiment disclosed, was variable; second, the molecular weights of biguanide and guanylurea are nearly the same; third, provided it is biguanide, the organic compound

suffers partial decomposition when the copper compound is dissolved in acid. Consequently, we decided to use the following procedure to determine the composition of the copper compound: the free organic base (either biguanide or guanylurea) was isolated from the copper compound, after which it was converted to the nitrate and identified in this form. The moist precipitate of copper compound was dissolved in hot 10% sulfuric acid; the crystals of the sulfate of the organic base that deposited on cooling were recrystallized from 5% sulfuric acid and then treated with a suspension of barium hydroxide in water; the obtained solution of the free base was neutralized with 2N nitric acid and then evaporated in vacuo at 5 mm until crystals of the nitrate were obtained; the latter were filtered, dried at 100°, recrystallized from methyl alcohol, and dried again. By means of preliminary experiments it was established that both biguanide and guanylurea are isolated from their copper compounds with such a procedure.

The obtained substance was identified as being biguanide nitrate; it contained 99.8% of biguanide nitrate and melted at 191° (melting point of biguanide nitrate is 192° [8]). To determine the amount of biguanide in the obtained nitrate we took 0.1 g of the nitrate and determined the amount of biguanide by precipitating it as the nickel compound [6].

To determine the amount of sulfuric acid in the copper compound we took 0.5 g of the substance, dried at 120° to constant weight [16], dissolved it in 10% hydrochloric acid, and precipitated the sulfate with barium chloride.

As a result, it was established that the precipitate of the copper compound contains copper biguanide sulfate, consequently, the intermediate reaction product in the formation of guanidine carbonate is biguanide.



Change in the amount of guanidine in the product obtained in the synthesis of guanidine carbonate as a function of the time of heating.

The fact that it is impossible to directly show the presence of biguanide in the synthesis product is explained by the instability of the former under the conditions of running the synthesis [17] (the transformation rate of biguanide into guanidine is greater than the formation rate of biguanide).

To study the mechanism of the reaction for the formation of urea we ran three experiments in small 12 ml autoclaves: in one case a mixture of ammonium bicarbonate, water, and liquid ammonia was charged into the autoclave, in the second case a mixture of cyanoguanidine, water, and liquid ammonia, and in the third case the reaction mixture consisted of cyanoguanidine, ammonium bicarbonate, water, and liquid ammonia; all of the substances were taken in the same amounts as when studying the kinetics of the reaction for the formation of guanidine carbonate. The autoclaves were heated in an oil bath to 130° and kept at this temperature for 30 minutes. Analysis of the obtained products revealed that the formation of urea occurs only in the presence of ammonium bicarbonate and does not depend on the presence of cyanoguanidine. As a result, under the conditions used to synthesize guanidine carbonate, urea is formed from ammonium bicarbonate, i.e., from ammonia and carbon dioxide.

SUMMARY

1. A study was made of the kinetics of the reaction for the formation of guanidine carbonate from cyanoguanidine, ammonium bicarbonate, and ammonia in aqueous solution in the temperature interval 100-150°.

2. The formation of guanidine proceeds through the formation of biguanide. The rate of biguanide formation is slower than the rate of its transformation into guanidine.

3. The amount of guanidine in the synthesis product increases with increase in the time of heating at a constant temperature; in this connection the rate of guanidine formation decreases. The maximum yield of guanidine corresponds to a heating period of 4 hours at 140°, and is equal to 40% of the theoretical yield.

4. Together with the main reaction for the formation of guanidine carbonate there proceed side reactions for the formation of hydroxyamino derivatives of 1,3,5-triazine, melamine and urea.

5. Urea is formed from ammonia and carbon dioxide under the conditions of synthesizing guanidine carbonate.

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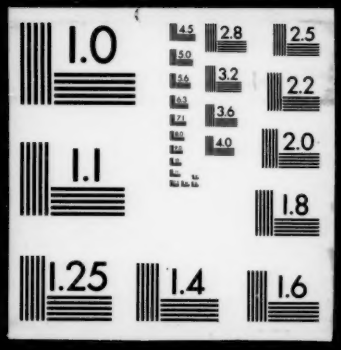
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